VOL. CLXIV, No. 4 OCTOBER, 1922 No. 607

Dr. W. W. Keen

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

COLLEGE OF PHYSICIANS OF PHILA. LIBRARY OCT 14 1922

THE CHARITY OF SURGERY MEDICAL BROWN JUN 3 1944

ESTABLISHED 1820

JOHN H. MUSSER, JR., M.D., EDITOR
[redacted] KRUMBHAAR, M.D., ASSOCIATE EDITOR

CLINICAL OBSERVATIONS ON BLOCK OF THE BRANCHES OF THE AURICULOVENTRICULAR BUNDLE. By JAMES B. HERRICK, M.D., and FRED M. SMITH, M.D. . 469

POST-TRAUMATIC CALCIFICATION OF THE PANCREAS, WITH DIABETES. By H. GIDEON WELLS, M.D. 479

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGIC POINT OF VIEW. By JOHN A. FORDYCE, M.D., ISADORE ROSEN, M.D., and C. N. MYERS, Ph.D. . 492

THE WASSERMANN REACTION IN NON-LUETIC CASES. By T. McKEAN DOWNS, M.D. 514

A FURTHER NOTE UPON A COMPARISON OF THE SACHS-GEORGI AND WASSERMANN REACTIONS IN THE SEROLOGIC DIAGNOSIS OF SYPHILIS. By ROBERT A. KILDUFFE, M.D. 523

TREATMENT OF SYPHILIS AMONG THE INSANE. By THOMAS B. CHRISTIAN, M.D. . 529

THE ROENTGEN-RAY DIAGNOSIS OF TUBERCULOUS CERVICAL LYMPH GLANDS. By JOHN MUNN HANFORD, M.D. 539

THREE CASES OF LEUKEMIA IN ONE FAMILY. By CHARLES W. McGAVRAN, M.D. . 545

THE CLINICAL SIGNIFICANCE OF TOTAL AND DIFFERENTIAL LEUKOCYTE COUNTS, WITH SPECIAL REFERENCE TO ACUTE INFECTIONS. By WALTER CLINTON JONES, M.D., and CLARA ENERIE BROWN 553

THE SURGERY OF THORACIC TUMORS. By ABRAHAM O. WILENSKY, M.D. . . 573

THE DIAGNOSIS AND TREATMENT OF AMEBIC COLITIS. By ALFRED C. REED, M.D. 587

INDEX TO ADVERTISERS . . . . . ADV. PAGE 34

Contents continued on page x

OWNERS AND PUBLISHERS

Philadelphia LEA & FEBIGER New York

COPYRIGHT, 1922, BY LEA & FEBIGER. ALL RIGHTS RESERVED. ENTERED AT THE POST-OFFICE AT PHILADELPHIA AS SECOND-CLASS MATTER

PUBLISHED MONTHLY. SUBSCRIPTION, SIX DOLLARS A YEAR, POSTPAID

BARNSTEAD WATER STILL

The most generally satisfactory water still on the market and used in the leading laboratories of the country.

Arranged for heating by gas, electricity, steam or kerosene as desired. Sizes from 1 pint per hour up. Write for bulletin giving full information.

EIMER & AMEND

Established 1851

Headquarters for Laboratory Apparatus and Chemicals

NEW YORK, N. Y.
Third Ave., 18th to 19th St.

WASHINGTON, D. C.
Display Room, Suite 601, Evening Star Bldg.

PITTSBURGH, PA.
4048 Jenkins Arcade

T
a

L

ry
ed
he

s,
as
er
ng

A.

The work of science is to substitute facts for appearances, and demonstrations for impressions.

—RUSKIN.

No prescription item can long survive that depends alone upon a catchy name, an attractive package and printer's ink for its good will and prestige. The medical profession wants facts with good appearance and demands results along with reading matter.

Oxyl-Iodide is a staple in the dispensing departments of good prescription stores practically everywhere. It is available for your prescriptions in bottles of 40 three-grain tablets and in dispensing bottles containing 500 tablets.

Oxyl-Iodide contains 33 per cent. of iodine in organic combination with phenylcinchoninic acid. It stimulates metabolism, promotes diuresis, and increases the elimination of uric acid and urea. It has proved particularly beneficial in stubborn types of chronic arthritis, neuritis, muscular rheumatism and gout. Send for literature.

All Lilly Products are Supplied Through the Drug Trade

ELI LILLY & COMPANY

INDIANAPOLIS, U. S. A.

IN THE ANNALS OF MEDICINE *and* BIOCHEMISTRY

they tell of the value of *YEAST THERAPY*

A prominent professor of therapeutics and doctor of medicine writes:

Is an antiseptic—increases resistance to certain infections—has laxative effect—checks fermentation. "Yeast.... is more or less of a gastro-intestinal antiseptic, increases the movements of the bowels, cleans a coated tongue, stimulates the production of white corpuscles, and often seems to aid in combating various streptococcic and staphylococcic infections. Hence it is a valuable treatment for septicemia and for boils and carbuncles.

"Besides the laxative effect of yeast, it has the ability to change the flora in the intestine and to more or less check fermentation. It should be much more frequently given in illness in which there is intestinal disturbance, especially if it is associated with constipation."

A professor in a great American University writes:

Rich in B-vitamin—beneficial effects. "The claim made for their use (yeast cakes) rests on a perfectly firm basis, they are rich in "B" vitamin, the proteins of the yeast cake are of good quality and the cake contains no ingredients poisonous to man. Many people are reporting beneficial effects from their use."

A noted professor and author of well-known text books says:

Food value of yeast—protein valuable. "The food value of yeast does not rest alone upon the vitamin present. The protein of the yeast is itself a very satisfactory type of protein so far as the nutrition of mammals is concerned. It is made use of in the tissues of man to as great an extent as is the protein of milk or meat, two of our most staple foods."

Send for free copy of the new brochure on Yeast Therapy. Use coupon, addressing THE FLEISCHMANN COMPANY, Dept. K-10, 701 Washington Street, New York, N. Y.

New brochure on yeast therapy sent on physician's request

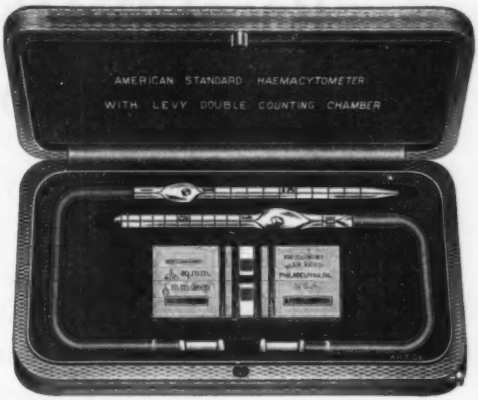
The Fleischmann Company
Dept. K-10
701 Washington St., New York

Please send me free a copy of the brochure on yeast based on the published findings of distinguished investigators.

Name.....
Street.....
City.....State.....

AMERICAN STANDARD
HAEMACYTOMETERS
WITH LEVY COUNTING CHAMBER

The Levy Counting Chamber was announced in November, 1916, patented January 31, 1917 (U. S. Patent No. 1,214,331) and was awarded the Edward Longstreth Medal of Merit by the Franklin Institute, Philadelphia, December, 1917



No. 3351. **American Standard Haemacytometer with Levy Counting Chamber with double Neubauer ruling**

THE LEVY COUNTING CHAMBER was the first dependable Haemacytometer Counting Chamber made in the U. S. and continues to be superior in several important characteristics to any chamber yet made either in Europe or America. Approximately 20,000 are now in use, without a single rejection because of inaccuracy.

It provides an increased visibility of ruling when the chamber is filled, unequalled by any ruling of European make, and a new method of construction of the parallel form of cell (first suggested by Bürker) which entirely avoids the cemented cell of the Thoma or Bürker construction with the attendant danger of separation from the slide.

The parallel or open form of chamber permits the filling of the ruled area on the cover-glass by capillary attraction **after the cover-glass is in position on the slide,** and provides a more uniform distribution of the corpuscles than is possible with the Thoma or circular form of counting chamber which is entirely closed by the cover-glass.

The dimensions of the ruling and the depth of the cell are guaranteed to be within the tolerances established by the Bureau of Standards and, when so ordered, Counting Chambers are furnished with Bureau of Standards certificate at an additional price.

		Code word
3350. **American Standard Haemacytometer,** complete with Levy Counting Chamber with Neubauer ruling, with two pipettes, in leather case	$15.00	*Darip*
3355. **ditto,** with Bureau of Standards certificate	20.50	*Datpy*
3351. **American Standard Haemacytometer,** same as No. 3350, but with Levy Counting Chamber with double Neubauer ruling	18.00	*Darvo*
3356. **ditto,** with Bureau of Standards certificate	24.50	*Daufs*

Copy of Supplement No. 53, "American Standard Haemacytometers" sent on request

---

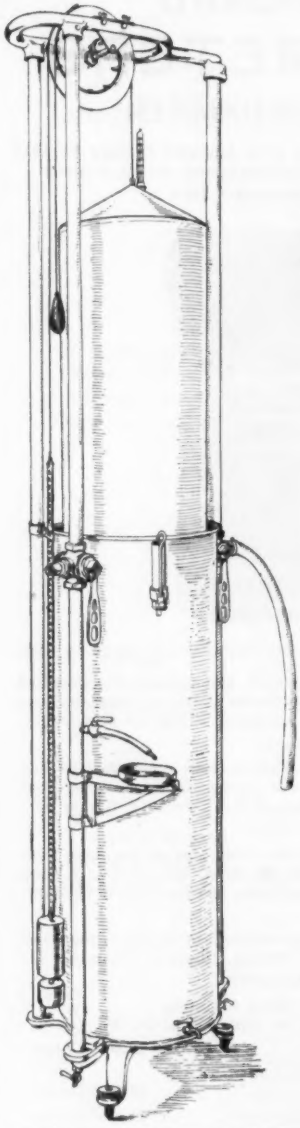
ARTHUR H. THOMAS COMPANY

WHOLESALE, RETAIL AND EXPORT MERCHANTS

LABORATORY APPARATUS AND REAGENTS

WEST WASHINGTON SQUARE — PHILADELPHIA, U. S. A.

CABLE ADDRESS, "BALANCE", PHILADELPHIA



AN OUTFIT

FOR

Basal Metabolism Estimations

AS DESIGNED BY

Dr. Cameron Vernon Bailey of the
Laboratory of Pathological Chemistry
New York Post Graduate Medical
School and Hospital

For detailed description see September issue
Journal of Laboratory and Clinical Medicine, 1921
or ask for reprint

AMERICAN MADE PRODUCTS

C. M. SORENSEN CO. NEW YORK
Tankless
AIR COMPRESSORS

REPRESENT QUALITY OF HIGHEST STANDARD

MANUFACTURED BY

C. M. SORENSEN CO., Inc.

DEPT. K

177 East 87th Street **New York**

Gastron

Submitted to the Physician

As a complete gastric gland extract, actually representative of the gastric-gland tissue juice in all its properties and activities, has found wide acceptance as an effective means of dealing with disorders of gastric function.

Of distinct service also as a detail of other treatment—through improved digestion, improved nutrition.

Gastron—an agreeable, stable solution
without sugar, without alcohol

Prescribed simply by the name—GASTRON

Fairchild Bros. & Foster
New York

For obtaining samples of blood for Wassermann tests. Patents pending. Copyright

An improvement on Dr. Albert Keidel's Original *Vacuum Blood Collector.*

IMPORTANT ADVANTAGES:—

Comer's Window Needle permits inspection of the breakable tip.

It is possible to **see** if the needle is properly introduced into the vein before breaking the tip of the ampoule. (The blood shows in the glass hub if the vein has been properly entered.)

The breakable tip is easily and **properly** broken by a quick, sharp bend.

The ampoule is of proper shape and size for the formation of the blood clot, and is **easily broken open** for removal of the sample.

The sample **can be centrifugated without being transferred to another tube.**

Each **Comer-Keidel** is a complete package which can be safely shipped in our special mailing case. It is sterilized for one hour at 150° C.

WE ALSO MAKE THE *ORIGINAL KEIDEL TUBE* AND ITS VARIOUS MODIFICATIONS

HARRIS COMER

Trading as STEELE GLASS COMPANY

622 S. Washington Square - - Philadelphia, Pa.

34 Years Experience Devising and Making Apparatus of Glass for Physicians, Chemists, Clinicians and Bacteriologists

Bloodpressure

Of what Value is it in Physical Diagnosis?

To quote the eminent Dr Crane, "It all depends" —upon you. Meaning that, in the final analysis, bloodpressure can be just what you want to make it.

GETTING back to fundamentals, the human body is a *living* thing just so long as the life blood circulates within it—and no longer The absence of circulation is death. Good health is largely a matter of efficient circulation, which in turn is primarily a matter of *pressure*. Was it the dawning of these basic facts that impelled the illustrious physiologist Ludwig to say that the discovery of bloodpressure was more important than that of the circulation?

Intelligent study of the circulation is, therefore, only possible if we accurately measure its causative *pressure*, not alone in the first instance, but every time we take it. And though the instrument employed is but one factor, let it be wrong and even the supremest effort may be nullified. Growing recognition of this fact has had much to do with the increasing importance of bloodpressure today.

You too can make "instrument variations" in bloodpressure a thing of the past, and get results of a kind you may never have thought possible—by using the

Baumanometer

"STANDARD FOR BLOODPRESSURE"

This precious reputation, first established by the force of sheer merit then ratified by the unanimous testimony of thousands of physicians—everywhere—who are now using it daily, bespeaks the everlasting accuracy perfect functioning and unfailing reliability of the Baumanometer

Our perpetual guarantee stands solidly back of every instrument we make, assuring complete and lasting satisfaction to the purchaser Should your dealer not have the Baumanometer in stock, write us and we will see that you are promptly supplied, no matter where you may be located.

Informative Literature Sent upon Request
Please Mention Your Dealer's Name

W. A. BAUM CO., INC.
100 FIFTH AVENUE, NEW YORK

A FEW REPRESENTATIVE PURCHASERS OF THE Baumanometer

Barker Dr. Lewellys F
Cabot, Dr. Richard
Christian, Dr. Henry A.
Janeway, Dr. Theo. C. (deceased)
Hare, Dr. Hobart
Lambert, Dr. Alexander
Tice, Dr. Frederick

◆

Battle Creek Sanitarium
Mayo Clinic
Rockefeller Foundation, China
Rockefeller Institute for Medical Research
United States Government (various departments)

◆

Columbia University
Cornell Medical College
Harvard University
Hahnemann Medical College
Johns Hopkins University
Yale Medical School

◆

Bellevue Hospital
Hahnemann Hospital
Loomis Sanitarium
Neurological Institute
Lakeside Hospital Cleveland
New York Hospital
Peter Bent Brigham Hospital

◆

American Telephone and Telegraph Company
Atlantic Coast Line R. R.
Carnegie Steel Works
General Chemical Company
Standard Oil Company
Tata Steel Works India
Union Pacific System

◆

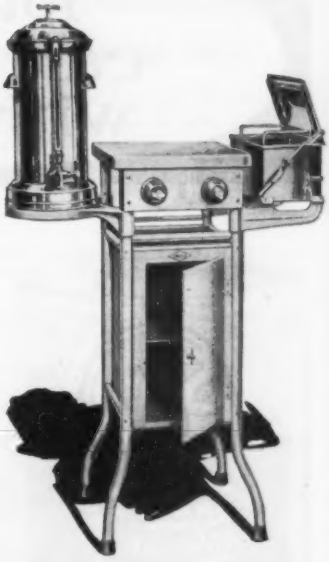
Equitable Life Assurance Society
First Mutual Life Tokyo Japan
*Metropolitan Life Insurance Co.
Mutual Life Insurance Co
New York Life Insurance Co
Northwestern Mutual Life Insurance Co

*The Metropolitan Life alone is using more than 1000 Baumanometers.

Good doctors like this

because—

It sterilizes water and instruments.
It has cabinet and treatment table.
Instruments can be removed by sterile hands.
Water in glass gauge is sterilized.
Electrically heated, it can't boil dry.
It impresses patients favorably.



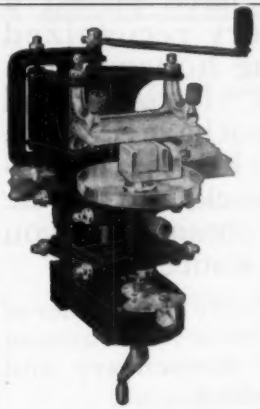
Your office may need just this sterilizer Send for catalog

CASTLE

No. 1413

WILMOT CASTLE COMPANY
1160 University Avenue Rochester, N. Y.
Makers of the largest line of Sterilizers for Physicians, Dentists and Hospitals

---



SPENCER CLINICAL MICROTOME
No. 880

FOR CELLOIDIN AND PARAFFIN AS WELL AS FROZEN SECTIONS

Automatic feed.
Covered and protected from dust and drippings.
Securely clamped to the table.
Cuts any desired thickness in multiples of 5 microns.
Unique knife-holder insures utilization of entire cutting edge of the knife.
Cuts very large sections.

No. 880 Microtome, complete with knife, $85.00
No. 930 CO_2 Freezing Attachment, $13.50

Used by MAYO BROS., Rochester, Minn., and by over two thousand hospitals, medical colleges and clinical laboratories

Prompt deliveries. Catalogue on request

SPENCER LENS COMPANY

MANUFACTURERS OF

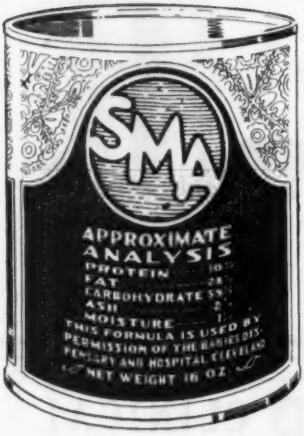
MICROSCOPES, MICROTOMES, DELINEASCOPES
OPTICAL MEASURING INSTRUMENTS, OPTICAL GLASS, SCIENTIFIC APPARATUS

BUFFALO, N. Y.

SPENCER BUFFALO U.S.A.

SPENCER BUFFALO U.S.A.

Your druggist can supply you with SMA



S. M. A. offers the family physician

(1) A simple and satisfying food for babies who are deprived of mother's milk, or who require food in addition to what the mother can supply.

(2) A food which requires only the addition of boiled water to prepare, whether for the month-old baby or the baby a year old.

(3) A food which contains the required food elements in proper proportion; and whose clinical records of feeding show an absence of spasmophilia and rickets in any infant fed with it while it was still well.

(4) A food which makes happy, solid, breast-fed-looking infants, and which insures normal development.

A Food to Keep Babies Well

Adapted to Mother's Milk

IN order to make S. M. A. easily accessible to all physicians, we have placed a supply in every recognized wholesale drug house in the United States. If your retail druggist does not have S. M. A., you can inform him that his jobber has it in stock, and that he can therefore obtain it for you on very short notice.

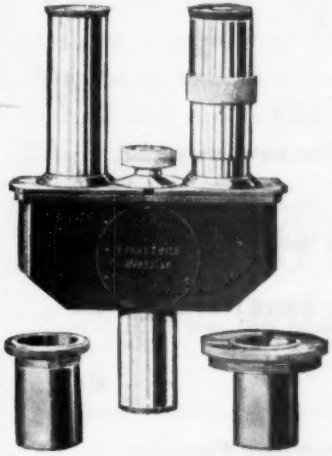
S. M. A. is sold only on the order of a physician. Formula by permission of The Babies' Dispensary and Hospital of Cleveland.

The Laboratory Products Company

3835 Cedar Ave. Cleveland, Ohio

Leitz Binocular-Stereo-Attachment

To Convert a Monocular Microscope into one for Binocular Vision



1. It can be used with any model of Leitz Microscopes.
2. With slight modification it can likewise be used with microscopes of other make.
3. It permits stereoscopic vision even with objectives of highest power (Oil Immersions).
4. It has means of adjustment to any interpupillary distance.
5. One eyepiece tube has focussing mount to permit the adjustment of difference in the refractive index between both eyes.
6. Removing the draw-tube of the microscope the Binocular attachment can simply be introduced in its place.

PRICE, $45.00

Write for Pamphlet No. L-1027

60 East E. LEITZ INC. NEW YORK 10th Street

Manufacturers, Wholesalers, Importers and Exporters in Laboratory Apparatus, Microscopical and Bacteriological Supplies
Organized under the Laws of the State of New York

"Sedatole"—"Linctus Comp."—"Hyotole"

three admirable demulcent expectorants of which ***we are now shipping large quantities*** to the drug trade in anticipation of your urgent requirements this fall and winter, when, owing to the shortage of coal, "flu," pneumonia, bronchitis, etc., are liable to occur in your practice, perhaps epidemically. If you send in for samples ***please mention your Federal License Number***—this only for our records. None needed when you prescribe them; just keep records.

SHARP & DOHME–Baltimore

Conscientious Chemists since '60

Ethical Expectorants

CONTENTS

ORIGINAL ARTICLES

Clinical Observations on Block of the Branches of the Auriculoventricular Bundle 469
By James B. Herrick, M.D., and Fred M. Smith, M.D., Chicago.

Post-traumatic Calcification of the Pancreas, with Diabetes 479
By H. Gideon Wells, M.D., Chicago.

Quantitative Studies in Syphilis from a Clinical and Biologic Point of View. 492
By John A. Fordyce, M.D., Isadore Rosen, M.D., and C. N. Myers, Ph.D., New York.

The Wassermann Reaction in Non-luetic Cases 514
By T. McKean Downs, M.D., Philadelphia.

A Further Note Upon a Comparison of the Sachs-Georgi and Wassermann Reactions in the Serologic Diagnosis of Syphilis 523
By Robert A. Kilduffe, M.D., Pittsburgh, Pa.

Treatment of Syphilis Among the Insane 529
By Thomas B. Christian, M.D., Morris Plains, N. J.

The Roentgen-ray Diagnosis of Tuberculous Cervical Lymph Glands . . 539
By John Munn Hanford, M.D., New York.

Three Cases of Leukemia in One Family 545
By Charles W. McGavran, M.D., Columbus, O.

The Clinical Significance of Total and Differential Leukocyte Counts, with Special Reference to Acute Infections 553
By Walter Clinton Jones, M.D., and Clara Enerie Brown, Birmingham, Ala.

The Surgery of Thoracic Tumors 573
By Abraham O. Wilensky, M.D., New York.

The Diagnosis and Treatment of Amebic Colitis 587
By Alfred C. Reed, M.D., San Francisco, Cal.

(Contents continued on page 12)

Trade Mark Registered.
Gluten Flour
40% GLUTEN
Guaranteed to comply in all respects to standard requirements of U. S. Dept. of Agriculture.
Manufactured by
FARWELL & RHINES
Watertown, N. Y.

THE REPUTATION AND INTEGRITY of the manufacturer is the physician's only guarantee of reliability of those organotherapeutic products for which there is no chemical or biological assay. Every manufacturing process and all our product is supervised by our Analytical and Research Department. When prescribing

ORGANOTHERAPEUTIC PRODUCTS

insure constancy and reliability of action by specifying

"G. W. CARNRICK CO."

Single Gland Products

Ovary	Thymus
Thyroid	Mammary
Pituitary—Entire	Prostate
Pituitary—Anterior	Orchic
Pituitary—Posterior	Parathyroid
Suprarenal	Pancreas
Corpus Luteum	Pineal
Spleen	Placenta

Special facilities for the manufacture of physicians' special formulae. Our Physicians' Service Department is maintained for coöperating with physicians in the problems of organotherapy

G. W. CARNRICK CO.

417-421 CANAL STREET NEW YORK, N.Y.

REVIEWS

Collected Papers of the Mayo Clinic. By Mrs. M. H. Mellish . . . 595
Vital Factors of Foods. By Carleton Ellis and Annie Louise MacLeod . 595
The Psychic Health of Jesus. By Walter E. Bundy, Ph.D. 596
The Principles of Electrotherapy and Their Practical Application. By W. J. Turrell 597
Studies in Influenza and Its Pulmonary Complications. By D. Barty King, O.B.E., M.A., M.D. (Edin.), M.R.C.P. (Lond. and Edin.) . 597
The Clinical Method in the Study of Disease. By R. M. Wilson, M.B., Ch.B. 598
Hyperpiesia and Hyperpiesis. By H. Batty Shaw, M.D., F.R.C.P. . . 598
Smell, Taste and the Allied Senses in the Vertebrates. By G. H. Parker 598
An Index of Treatment by Various Writers. Edited by Robert Hutchinson, M.D., F.R.C.P., and James Sherren, C.B.E., F.R.C.S. Revised to conform with American usage by Warren Coleman, M.D. . . . 599
Glands in Health and Disease. By Benjamin Harrow, Ph.D. 600
Epidemiology and Public Health. Volume I, Respiratory Infections. By Victor C. Vaughan, M.D., LL.D., assisted by Henry F. Vaughan, M.S., Dr. P.H., and George T. Palmer, M.S., Dr. P.H. 600
Studies in Neurology. By Henry Head, M.D., F.R.S. 601
Venereal Clinic. By Ernest R. T. Clarkson, M.R.C.S. 602

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., ROGER S. MORRIS, M.D.,
AND
THOMAS ORDWAY, M.D.

Megacaryocytes in Circulation 603
The Blood Sugar After Removal of the Liver 603
Capillary Blood-pressure in Arterial Hypertension 604
Studies on Blood Cholesterol in Syphilis 604
The Role of Agglutination in the Immediate Toxic Effects of Arsphenamine 604
A Serological Study of Hemolytic Streptococci 605
Remote Prognosis in War Nephritis 605
Radium Emanations in Exophthalmic Goiter 605

(*Contents continued on page 14*)

ALLONAL "Roche"
A new NON-NARCOTIC Drug
which is both
HYPNOTIC and ANALGESIC
Supplies and Literature will be furnished on request
The HOFFMANN-LA ROCHE CHEMICAL WORKS
New York

The PREMIER Product of
Posterior Pituitary active principle

Armour's LABORATORY PRODUCTS

Headquarters for the ENDOCRINES

PITUITARY LIQUID
(Armour)

free from preservatives, physiologically standardized.

1 c.c. ampoules surgical, ½ c.c. obstetrical. Boxes of six.

A reliable oxytocic, indicated in surgical shock and post partum hemorrhage, and after abdominal operations to restore peristalsis.

Suprarenalin Solution
1:1000—Astringent and Hemostatic

Water-white, stable. In 1-oz. bottles, with cup stopper. Of much service in minor surgery. E.E.N. and T. work.

ARMOUR AND COMPANY
CHICAGO

WILLIAM SCHEPPEGRELL, A.M., M.D.
President American Hayfever Prevention Association.
Chief of Hayfever Clinic, Charity Hospital, New Orleans

Says:—

"IF the patient applies for treatment during an attack of hayfever, the pollen extracts are usually ineffective, and a vaccine should be used, these being injected at intervals of one or two days until the severity of the attack subsides."*

The Vaccine used by Dr. Scheppegrell is practically identical with Sherman's No. 36 which is being extensively used in the prophylaxis and treatment of Hayfever.

*From Dr. William Scheppegrell's new book on Hayfever and Asthma, Lea & Febiger, Publishers

---

Bacteriological Laboratories of
G. H. SHERMAN, M.D.
DETROIT, MICH.

CONTENTS—(*Continued*)

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

Thoracoscopy in Surgery of the Chest 606
Gross Pathology of Brachial Plexus Injuries 606
Surgical Anatomy of the Trigeminal Nerve 606
Secondary Parotitis 607
A Study of Sixty-five Cases Seeking Relief After Short-circuiting Operations 607
Ascending Infections of the Kidney 607
Gastric Syphilis 608
Nature and Cause of Old-age Enlargement of the Prostate 608
Anomalous Abdominal Membranes 608
Clinical Aspects of Abdominal Tuberculosis 609
The Treatment of Surgical Tuberculosis with the Carbon-arc Lamp . . 609
Tuberculous Abscesses of the Chest Wall 609

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.

Acute Infections and Contagious Diseases in Childhood in the Etiology of Cardiovascular Disease in the Adult 610
Results of Active Immunization with Diphtheria Toxin-antitoxin in the Public Schools of New York City 610
The Food Requirements of Children: Fat Requirement 611
Milk Ingestion in Relation to Changes in Body Weight in Newborn Infants 612
Observations on the Heart in Mothers and the Newborn 612
The Severe Blood Diseases of Childhood 613

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Chemical Observations on the Toxemias of Pregnancy 614
A Sign of Intrauterine Death 614
Labor Complicated by Infected Fibroid 615
Induction of Labor with Castor Oil and Quinine 615
Rupture of the Uterus through a Cesarean Scar 616
Twin Pregnancy and the Diagnosis of Superfetation 616
Blood-pressure in Pregnancy 617

(*Contents continued on page 16*)

AGOCHOLAN STRONTIUM CHOLOSALICYLATE

FOR THE TREATMENT OF BILIARY AND HEPATIC DISORDERS
A PROPHYLACTIC IN THE DISPOSITION TO CHOLELITHIASIS

Vials of 50 and tubes of 20
Sugarcoated Tablets
Two grains each

For Sale by
MERCK & CO.
NEW YORK ST. LOUIS

Samples and full literature from
E. BILHUBER, INC.
25 WEST BROADWAY, NEW YORK

IN JANUARY, 1917

THE BACILLUS ACIDOPHILUS

was introduced and made available to the medical profession

FOR THE FIRST TIME

through

BACID PREPARATIONS

which were created solely to make possible the therapeutic use *of* this antiputrefactive organism the Normal Habitat of which is the Human Intestine in health

BACID PREPARATIONS

TABLETS—CAPSULES—LIQUID CULTURES

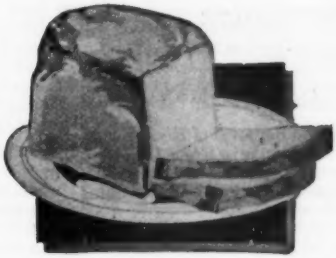
do **not now** and **never have** contained the B. bulgaricus—either Type A or Type B

LITERATURE—BIBLIOGRAPHY—ON REQUEST

Guaranteed and Manufactured ONLY by

THE ARLINGTON CHEMICAL COMPANY

YONKERS, N. Y.



Starch-*free* Bread

A real adjunct in the management of

DIABETES

STRICTLY NON-CARBOHYDRATE BREAD, MUFFINS, BISCUITS, PASTRY, ETC., CAN BE MADE EASILY BY YOUR PATIENTS FROM

Put up in carefully measured boxes one for each day

A month's supply (30 boxes) $4.85

LISTERS
PREPARED CASEIN
DIABETIC Flour

Sold by leading druggists or sent directly to your patients with easily followed recipes

Made by LISTER BROS., Inc., 405 Lexington Ave., New York

CONTENTS—(*Continued*)

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D., AND FRANK B. BLOCK, M.D.

Elephantiasis Vulvæ 617
Action of Emetin Hydrochloride upon the Uterus 619
Radium Treatment of Benign Bleeding 619

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M., AND DE WAYNE G. RICHEY, B.S., M.D.

The Action of Neoarsphenamine and Neosalvarsan on the Phagocytic Activity of Leukocytes 621
Studies on the Nature of the Action of Nonspecific Protein in Disease Processes: III. Nonspecific Proteins and Soluble Toxin 621
An Experimental Study of the Effects of Protein Injections upon Infections 622
Frequency of Bacillus Influenza in the Nose and Throat in Acute Lobar Pneumonia 622

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D. AND GEORGE W. McCOY, M.D.

Carbon Tetrachloride: A Drug Proposed for the Removal of Hookworms, with Special Reference to its Toxicity for Monkeys when Given by Stomach Tube in Repeated Doses 623
A Rapid Method of Determining the Presence and Type of Botulinus Toxin in Contaminated Foods 624
Smallpox in Twenty States 624

Now obtainable in Ampuls

Physiologically Standardized Digitannoids

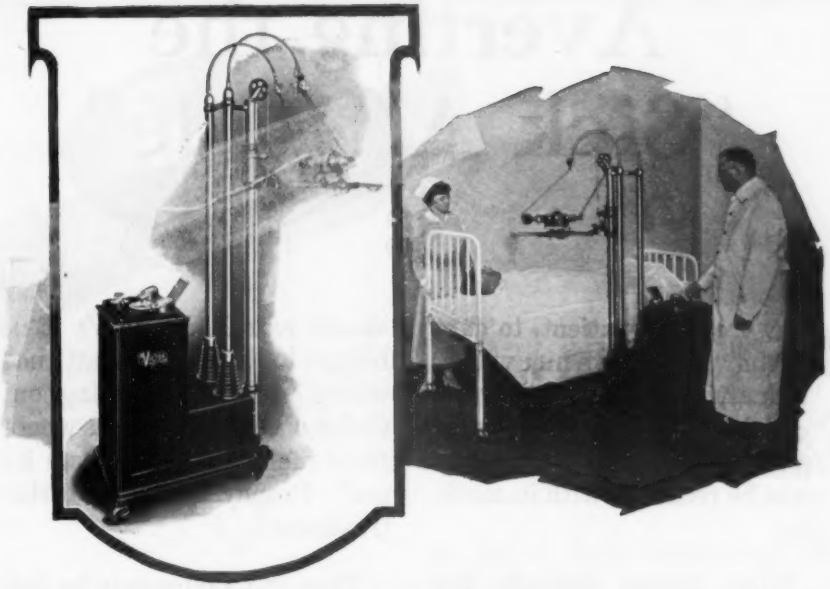
Digitan

Originally Introduced as *Digipuratum*

For circulatory disturbances. In surgery to sustain heart action

Ampuls: 1 Cc. each, boxes of 6
Powder: In vials of ¼ oz.
Tablets: 1½ grains, tubes of 12
Oral Solution: Vials of 12 Cc.

MERCK & CO.
New York



This New Victor X-Ray Outfit Is Radically Different

It Is a *Stabilized* Mobile Unit

What the Stabilizer Does

When the voltage of the line supply current fluctuates (this condition prevails on practically every line) the Victor-Kearsley Stabilizer, incorporated in this unit, acts *automatically* to hold the milliamperage constant in the Coolidge Tube—the exact milliamperage desired for the radiograph. 100% radiographic results are therefore insured—no "retakes" necessary because of fluctuating line supply.

Control Features

Auto-transformer allows selection of any penetration desired from 3 to 5 inches, divided into 26 steps—a fineness of graduation that is distinctive in this outfit. The stabilizer permits selection of any milliamperage from 2 to 30, at any setting of the auto-transformer. A chart on the control board helps the operator to obtain instantly any current value.

Circuit Breaker Safety Device

In case of "overload" beyond the capacity of the tube (30 Ma. at 5" back-up spark) this device *automatically* shuts off current supply, preventing damage to tube and apparatus. Consider also the importance of this from the standpoint of protection to both operator and patient, in case of accidental contact with the high tension system.

A Complete X-Ray Unit

Where only limited space is available in the physician's office, the compactness of the Victor Stabilized Mobile X-Ray Unit solves the problem. Mounted on casters and easily moved about, it lends itself to varied demands. It also becomes an extremely valuable addition to any existing hospital equipment.

The Victor-Kearsley Stabilizer is one of the most important X-Ray developments since the advent of the Coolidge Tube itself. It should not be confused with other devices which tend to stabilize only the current to the filament of the tube. The important advantages of this unit are fully explained in a special bulletin, which we will gladly send you on request.

VICTOR X-RAY CORPORATION, Jackson Blvd. at Robey St., Chicago

Sales Offices and Service Stations in All Principal Cities

VICTOR

Averting the "Sick Attitude"

TO treat the patient, to cure him, yet to leave him with a "sick attitude," is sounding the "call back" before the fire is fully extinguished. Psychology must be reckoned with in medicine.

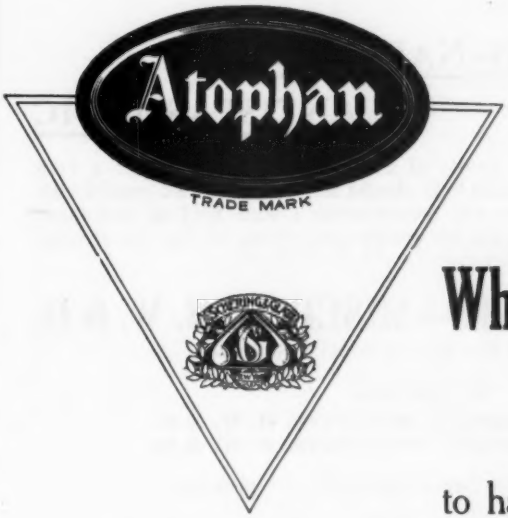
What flashes through the mind of your patient when you pronounce: "Cut out Coffee!" Doesn't that patient's mind immediately interpret that dictum as "I'm seriously sick!"

Perhaps he is; perhaps his case *is* one of the *very few* in which Coffee *may* be contra-indicated. Then, certainly, rule it out. But why make the pronouncement a *general* one without first determining the facts, without first determining that the etiology, the symptomatology, the diagnosis of each individual case point to Coffee as even a *possible* pathologic factor? Doesn't such a course tend toward a "sick attitude" in many, many cases where none should exist? Wouldn't it be better to avert this attitude where possible by ruling out Coffee *only* in those cases where facts really contra-indicate its use? Prophylaxis is the better treatment!

Then, too, Coffee may be just the therapeutic aid you seek. For instance, Dr. Walter A. Bastedo, of Columbia University, in his book, *Materia Medica, Pharmacology, Therapeutics, and Prescription-Writing*, says: "Coffee results in a prompt increase in the amount and the acidity of gastric juice, and it is a well-known fact that on the intestines the beverage acts as a laxative, promoting peristalsis."

Cutting Coffee from the regimen suggests seriousness to the patient. Why do it without warrant in fact? Adding Coffee to your armamentarium is profiting by the experience of others.

Joint Coffee Trade Publicity Committee, 64 Water Street, New York, N. Y.



What shall it profit the patients?

Rheumatism
Gout
Neuralgia
Neuritis
Sciatica
Lumbago
Migraine

to have their sufferings relieved, if it's done by throwing into their most vital body machinery a monkey wrench like colchicum, the salicylates, or the old time coal-tar derivatives—heart-depressants, kidney-irritants, intestine-disturbants.

Genuine ATOPHAN, devoid of all these drawbacks, is manufactured at our Bloomfield, N. J., plant by a special process, precluding the possibility of even traces of unpleasant empyreumatic admixtures

Complimentary Trial Package and Information From

SCHERING & GLATZ, Inc.

150-152 Maiden Lane **NEW YORK**

Averting the "Sick Attitude"

TO treat the patient, to cure him, yet to leave him with a "sick attitude," is sounding the "call back" before the fire is fully extinguished. Psychology must be reckoned with in medicine.

What flashes through the mind of your patient when you pronounce: "Cut out Coffee!" Doesn't that patient's mind immediately interpret that dictum as "I'm seriously sick!"

Perhaps he is; perhaps his case *is* one of the *very few* in which Coffee *may* be contra-indicated. Then, certainly, rule it out. But why make the pronouncement a *general* one without first determining the facts, without first determining that the etiology, the symptomatology, the diagnosis of each individual case point to Coffee as even a *possible* pathologic factor? Doesn't such a course tend toward a "sick attitude" in many, many cases where none should exist? Wouldn't it be better to avert this attitude where possible by ruling out Coffee *only* in those cases where facts really contra-indicate its use? Prophylaxis is the better treatment!

Then, too, Coffee may be just the therapeutic aid you seek. For instance, Dr. Walter A. Bastedo, of Columbia University, in his book, *Materia Medica, Pharmacology, Therapeutics, and Prescription-Writing*, says: "Coffee results in a prompt increase in the amount and the acidity of gastric juice, and it is a well-known fact that on the intestines the beverage acts as a laxative, promoting peristalsis."

Cutting Coffee from the regimen suggests seriousness to the patient. Why do it without warrant in fact? Adding Coffee to your armamentarium is profiting by the experience of others.

Joint Coffee Trade Publicity Committee, 64 Water Street, New York, N. Y.

Atophan

TRADE MARK

What shall it profit the patients?

Rheumatism
Gout
Neuralgia
Neuritis
Sciatica
Lumbago
Migraine

to have their sufferings relieved, if it's done by throwing into their most vital body machinery a monkey wrench like colchicum, the salicylates, or the old time coal-tar derivatives—heart-depressants, kidney-irritants, intestine-disturbants.

Genuine ATOPHAN, devoid of all these drawbacks, is manufactured at our Bloomfield, N. J., plant by a special process, precluding the possibility of even traces of unpleasant empyreumatic admixtures

Complimentary Trial Package and Information From

SCHERING & GLATZ, Inc.

150-152 Maiden Lane **NEW YORK**

A NON-TOXIC

NON-NARCOTIC

ANTISPASMODIC

which, when used within the limits of its indications, will render a very satisfactory percentage of results. It should not be prescribed empirically, but a proper selection of cases will demonstrate a wide field of usefulness. It is only an effective relief agent for spastic conditions of the non-striated muscles, and not a general sedative.

BENZYL BENZOATE—MISCIBLE, H. W. & D.

(The Original and Most Efficient Benzyl Antispasmodic)

We also offer

GLOBULES OF BENZYL BENZOATE, H. W. & D.
TABLETS OF BENZYL SUCCINATE, H. W. & D.

LITERATURE AND TRIAL PACKAGES ON REQUEST

H. W. & D.—*Specify*—H. W. & D.

HYNSON, WESTCOTT & DUNNING, Baltimore

Miss Harris' Florida School

Porch Fronting Biscayne Bay

FOR those recovering from illness the climate is ideal, also for those for whom northern winters are rather severe. No student can be admitted, however, whose state of health would, in any way, be a source of danger to others.

School under northern management, the faculty all being graduates of northern colleges. There is, therefore, no break in system for pupils coming south for full year or season. Tourist pupils follow courses of home schools. Intermediate and high school. Boarding and day school departments.

Outdoor classes, ocean bathing and golf throughout the winter

Physician's certificate of health required before admission

FOR CATALOGUE, ADDRESS 1067 BRICKELL AVENUE

MIAMI, FLORIDA

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

OCTOBER, 1922

ORIGINAL ARTICLES.

CLINICAL OBSERVATIONS ON BLOCK OF THE BRANCHES OF THE AURICULOVENTRICULAR BUNDLE.

By James B. Herrick, M.D.,

and

Fred M. Smith, M.D.,

Chicago.

This report is based on clinical observations that were made on thirty-five patients in each of whom the probable diagnosis of bundle branch block was made from the electrocardiogram. The *QRS* group was atypical in each of the three leads and exceeded 0.1 second in duration. Some of these patients came under observation during the time that studies[1] [2] were being made on experimental lesions of the branches of the auriculoventricular bundle of the dog, so that in this clinical study it was natural to attempt to correlate as nearly as possible the electrocardiographic findings with those produced experimentally in the dog.

Age Incidence. Twelve patients were in the fifth and 13 in the sixth decade of life; 6 were under fifty and 4 above seventy; 20 were between fifty-five and sixty-five years. The youngest patient was twenty-three years old.

Possible Etiological Factors. In 17 there was an associated chronic nephritis. Five had arterial hypertension with negative urinary findings. The blood Wassermann test was made in 10. In five of these the reaction was positive. Each of these gave a history of having had a chancre. It was noted that the age incidence in these 5 was below fifty years. Ten gave histories of having

had inflammatory rheumatism. Five had been addicted to alcohol and 2 had had typhoid fever.

Symptoms. Eighteen were short of breath on slight exertion. Seventeen had difficult breathing even when at rest. In 8 the duration of the shortness of breath had existed for more than two years, in 10 more than one year and in the remaining 17 less than one year. Twelve had cardiac asthma. Ten gave histories of having anginal pain. In 4 of these the pain had at one time been very severe, lasting several hours, and morphin was required for relief. Twenty had noticed swelling of the feet.

Physical Findings. In every instance the cardiac dulness was increased to the left. Twenty-five had an apical systolic murmur. Ten had a systolic murmur over the aortic area. Only one had the diastolic murmur of aortic regurgitation. This patient had a distinct widening of the aorta. Twelve had gallop rhythm. A muffled first tone was a common finding. Twenty had rales in the bases of the lungs, a palpable liver and some edema of the ankles. Twenty-three had a systolic blood-pressure ranging from 175 to 250. In eight of these a *pulsus alternans* was noted. Seventeen had albumin and granular and hyaline casts in the urine.

Clinical Course Since First Seen by Us. We have been able to follow 21 of these patients. Twelve died within eighteen months after the first examination. The average duration of life was less than one year. Ten died from cardiac failure. One of these died suddenly following recovery from a prostatectomy, presumably a coronary accident. Another after a cataract operation died from a thrombosis of the cerebral arteries. The youngest patient of the series died on the same day after the resection of the left fifth rib for an adhesive pericarditis. The clinical diagnosis of extensive cardiac hypertrophy, adhesive pericarditis, double mitral lesion, tricuspid regurgitation, fibrous myocarditis and cirrhosis of the liver was verified by necropsy. Autopsies were done in 2 other cases in which an extensive sclerosis of the coronary arteries and a disseminated myocardial fibrosis were found. In neither case was the conduction system examined histologically. Six of the 10 patients that are known to be alive are in bad condition. Two of them have had major operations. Following the operations they had very stormy periods of cardiac upset. Since recovery the clinical manifestations of cardiac weakness have rapidly progressed. Four patients have reported that they were improved.

Electrocardiographic Findings. The prevailing ventricular phases were broad at the base and notched or slurred near or at the apex. The duration of the *QRS* group in all instances exceeded 0.1 second and in many the duration approached 0.15 second. The *T*-wave assumed a direction opposite to that of the most prominent ventricular deflection. In thirty-two instances the chief ventricular wave (Fig. 1, top) was positive in lead I and negative in lead III.

2536 C 1 29 My 44

In the remaining three the *S*-wave was the most prominent wave in lead I and the *R*-wave in lead III (Fig. 1, bottom).

The fiber of the galvanometer was standardized so that 3 millvts. caused a deflection of 30 mm. In 12 the amplitude of both the *R*

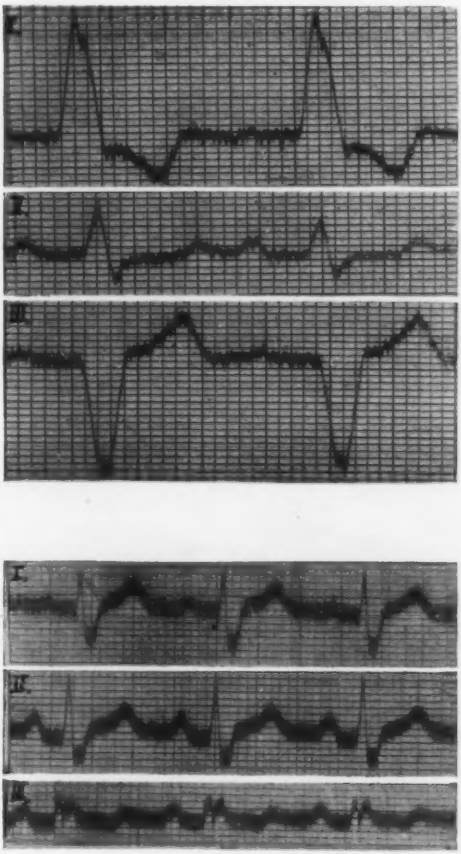


FIG. 1.—*Top:* The prevailing ventricular phase is positive in leads I and II and negative in III; it is blunt or slurred at the apex, and its duration is about 0.14 second. *Bottom:* The chief ventricular deflection is negative in lead I and positive in lead III. The duration of the *QRS* group is about 0.12 second.

and the *S* deflections was large and in 10 small. In 3 the amplitude of the low deflection curves increased while the patients were under observation. One of these patients has been studied over a period of one year. During this time electrocardiograms have been taken at frequent intervals. When first seen he was orthopneic, had

passive congestion of the lungs, engorgement of the liver and edema of the ankles. He had a systolic murmur at the apex and a gallop rhythm. The systolic blood-pressure was 238 and the diastolic 120. There was a *pulsus alternans*. He was kept in the hospital until the heart improved and afterward rested at home four months. The initial electrocardiogram (Fig. 2) shows very atypical broad *R* and *S* deflections of low amplitude. In

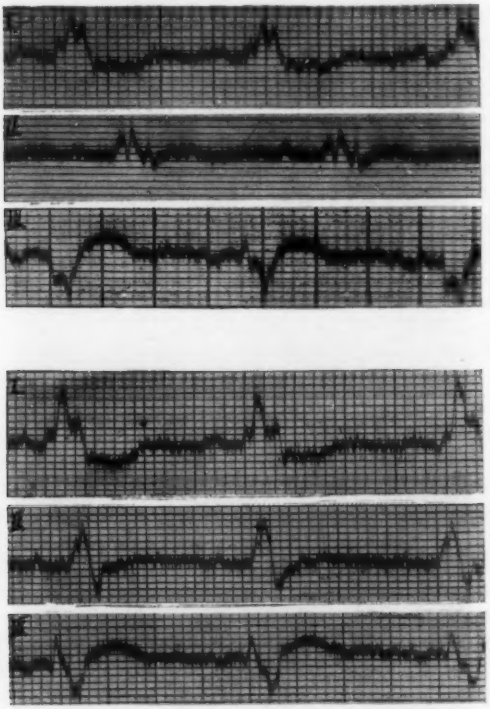


FIG. 2.—*Top:* Initial electrocardiogram taken December 20, 1919. *Bottom:* This electrocardiogram was taken January 5, 1920. The patient had been at rest in bed for two weeks.

the later electrocardiograms (Figs. 2, 3, 4) the *R* and *S* waves become less atypical and their amplitude gradually increases. In the last record (Fig. 4) the prevailing ventricular deflection is tall and resembles that of a left ventricular preponderance. The duration of the *QRS* group is, however, still prolonged. This change in the electrocardiogram was coincident with the clinical improvement of the patient. He was relatively free from cardiac symptoms for three months, and during that time worked as a

presser. Later he became short of breath again and the amplitude of the ventricular deflections decreased. He is at present in the hospital in a critical condition. The electrocardiogram now is similar to that when first seen.

The electrocardiogram (Fig. 5) in one case showed some *QRS* groups that approached the normal in duration. We were able

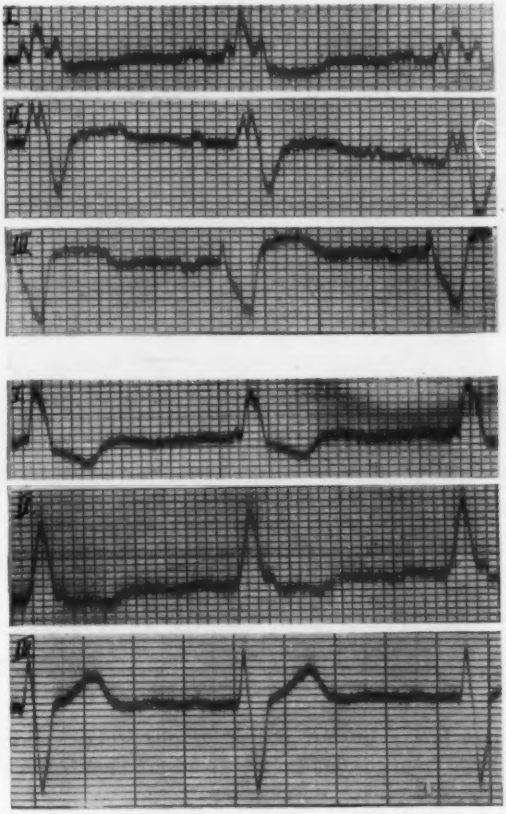


FIG. 3.—*Top:* Electrocardiogram taken April 14, 1920. *Bottom:* Electrocardiogram taken June 21, 1920.

to follow this case, and the *R*-waves of leads I and II were later apparently normal in duration, while the *S*-wave in lead III was slightly broad (Fig. 5, bottom). When first seen at the cardiac clinic of the Central Free Dispensary this patient was in an extremely bad condition. She was cyanotic and very dyspneic. The heart-rate was about 120 per minute and the auricles were fibrillating.

The electrocardiogram taken at this time is shown in Fig. 5 (upper tracings). She returned to the clinic two weeks later. She was then markedly improved. The heart-rate was about 65 per minute and she could walk fairly comfortably. The electrocardiogram shown in Fig. 5, (lower) was taken at this time.

Three patients produced electrocardiograms in which the *PR* interval was slightly more than 0.2 second. Three had heart-block. In one of these the partial block of the main stem was transient (Fig. 6). In leads I and III there is seen a 2-1 auriculo-ventricular ratio. In lead II all the sinus impulses are passing over the bundle. The transmission period is, however, prolonged.

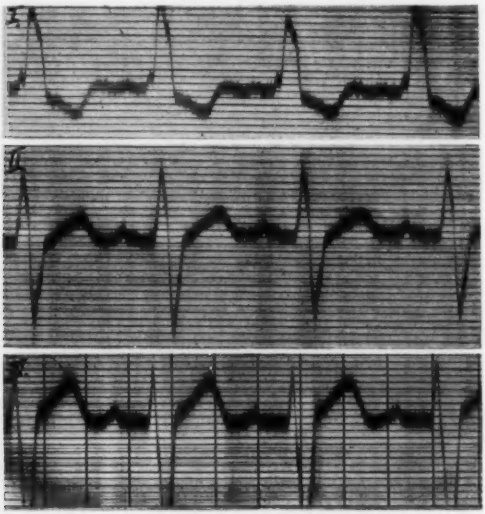


FIG. 4.—This record was made in October, 1920. The chief ventricular deflection is now tall and less atypical.

This patient had many attacks of Adams-Stokes syndrome and died suddenly from cardiac failure about six months following the time this electrocardiogram was taken.

In 5 instances there were auricular fibrillations.

Comment. All the patients of this series had symptoms and physical findings indicative of cardiac weakness. In 17 (48.5 per cent) these manifestations of weakness were very marked. That the outlook is poor is shown by the clinical course following the first examination. Eleven (52.3 per cent) of the 21 whose subsequent history was followed died within eighteen months, the average duration of life being less than one year. This mortality is in accord with the figures of other observers. Willius[3]

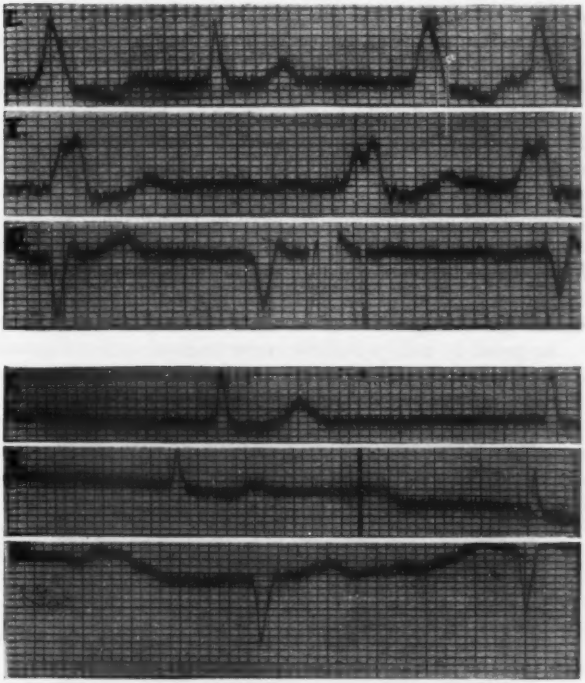


FIG. 5.—*Top:* Initial electrocardiogram; a few of the prevailing ventricular phases have an approximately normal duration; the others are very atypical and have a duration of about 0.15 second. *Bottom:* This electrocardiogram was taken two weeks later. The clinical condition of the patient was markedly improved.

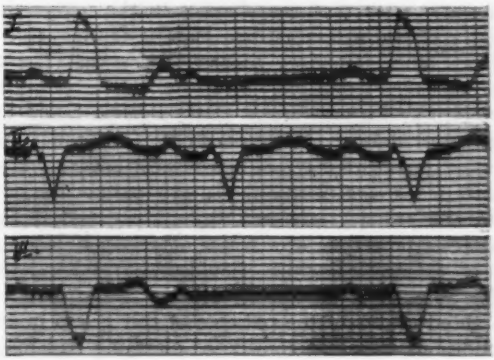


FIG. 6.—Leads I and III show 2–1 block. In lead II the auriculoventricular ratio is 1–1. The *PR* interval is, however, prolonged.

reported a mortality of 69.6 per cent in a series of 112 cases. The average duration of life in his cases from the time of examination was eight and one-half months. Forty-eight per cent of those studied by Oppenheimer and Rothschild[4] died within two years.

In those instances in which autopsies have been made there has usually been found an advanced sclerosis of the coronary arteries and extensive fibrous myocardial changes. The necropsy findings of 2 cases of this series, of 4 reported by Willius[3] and of 12 studied by Oppenheimer and Rothschild[4] were of this type. In 8 of the fourteen autopsies reported by Oppenheimer and Rothschild[4] there was found an occlusion of the anterior descending branch of the left coronary artery. Four of the cases of our series had severe attacks of anginal pain, suggestive of coronary artery accident, though there is no proof by autopsy of the correctness of such a diagnosis.[5 6]

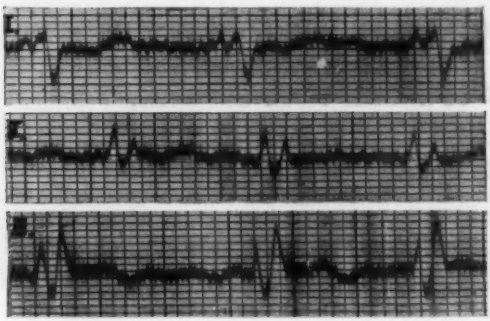


FIG. 7.—Shows very atypical *QRS* group. The duration is about 0.1 second.

It is to be noted from the histories, clinical findings and autopsy reports of these cases that the changes in the myocardium in a vast majority of the instances are chronic, degenerative in character and are often secondary to arteriosclerosis. The muscular changes are usually extensive. It is for this reason that these types of electrocardiograms are so rarely seen in cases of primary valvular disease. Only one instance of chronic valvular disease has been observed by us that gave an electrocardiogram (Fig. 7) similar to those under consideration. In this patient the myocardial invasion by the primary infection was quite extensive (autopsy).

Any operative procedure of a major character in a patient with this type of electrocardiogram should be considered dangerous even in the absence of advanced clinical cardiac manifestations. It will be noted that 3 of the patients of this group in whom the cardiac conditions were not considered alarming had major operations. Two had very difficult recoveries from cardiac upsets which developed rapidly after the operation. One died suddenly

following the recovery from a prostatectomy, from what seemed to be a cardiac accident. Another died following operation for cataract from thrombosis of the cerebral arteries and of one femoral vein. Another died on the same day after the resection of the left fifth rib for an adhesive pericarditis.

The long duration of the *QRS* group and the direction assumed by the final deflection of these electrocardiograms probably indicate in most instances a block of the impulse over one branch or over a majority of the subdivisions of one branch of the auriculoventricular bundle. These conclusions are in harmony with experimental observations on the dog.[7 8 1 2] In the dog electrocardiograms characteristic of right or left branch block were produced only when these respective branches or a majority of the subdivisions of these branches were divided. The division of the arborization branches alone did not change the electrocardiogram.[7 8 1 2] There were some instances, however, following the cutting of the smaller ramifications to the left ventricle in which the electrocardiogram became atypical after the left ventricle was weakened and dilated as the result of the ligation of branches of the left coronary arteries. In some the electrocardiogram returned to normal after the ligatures were removed from the arteries.[2]

In 32 cases the electrocardiograms conform to the type usually considered as representing defects of the right division. The reasons for making a probable anatomic diagnosis on the basis of this type of electrocardiogram have been considered by one of us in a former report.[2] In this connection, however, it would seem that these points again deserve brief mention. The electrocardiograms under consideration resemble those produced experimentally in the dog by the division of the right branch of the auriculoventricular bundle. This is considered by Lewis[9] as the most convincing reason for making a probable anatomic diagnosis in man on the basis of the electrocardiographic findings. Furthermore, cases have been reported by Eppinger and Stoerk,[10] Cohn and Lewis[11] and Lewis[9] in which the suspected lesion of the right branch was found by histologic examination. Yet Cohn and Lewis[12] found no lesions of the right branch in four instances. In discussing these findings they suggested the possibility of a functional block [13 14 15 16] or in some instances of block of the main stem. Oppenheimer and Pardee[17] have recently recorded two cases in which the lesions were found in the branch other than that anticipated from the electrocardiograms. The findings in one of these cases are not sufficient to offset the above evidence. Further investigation along this line is desirable.

In one instance (Fig. 5, top) the duration of the *QRS* groups varied from 0.06 to 0.15 second. It is assumed that these findings represent a variation in the extent of the interventricular con-

duction defect. The possibility of incomplete bundle branch block was considered.

Three cases produced electrocardiograms in which the chief ventricular deflection was negative in lead I and positive in lead III. This type of electrocardiogram has been held to represent a defect of the left branch. This conception is not supported by experimental studies on the dog but is apparently based solely on a few clinical observations.

Summary. 1. Thirty-five cases were studied in which the electrocardiographic findings probably indicate a block of one main branch, or the majority of the subdivisions of one main branch, of the auriculoventricular bundle. The *QRS* groups were atypical in the three leads and exceeded 0.1 second in duration. In many the duration approached 0.15 second. The *T*-wave assumed the direction opposite to that of the prevailing ventricular deflection.

2. In 32 the prevailing ventricular deflection was positive in lead I and negative in lead II and the duration of the *QRS* was prolonged and in many instances approached 0.15 second duration. These electrocardiograms probably represent defects of the right branch.

3. In 3 cases there was an *S*-wave in lead I and *R*-wave in lead III. In these cases the location of the probable lesion of the conduction system is uncertain.

4. In some instances there was a change in the form of the *QRS* group which was coincident with the clinical improvement of the patients. In three there was an increase in the amplitude of the chief ventricular deflections. In one the atypical *QRS* groups disappeared except for a slight increase in duration of the *S*-wave in lead III.

5. All of these patients had symptoms of myocardial weakness. In 17, or 48.5 per cent, there were clinical manifestations of advanced cardiac disease. In nearly all instances the cardiac weakness seemed to be due to a slow degenerative change in the myocardium secondary to arteriosclerosis. Twelve, or 57.1 per cent, of the 21 patients that we were able to follow died within eighteen months. Ten of them died from cardiac failure. Autopsies were done in 3. In 2 there was an extensive sclerosis of the coronary arteries and marked myocardial fibrosis. In the other the anatomic diagnosis was obliterative pericarditis—huge dilatation and hypertrophy of the right auricle and ventricle, moderate hypertrophy of the left ventricle, myocardial fibrosis and cirrhosis of the liver.

BIBLIOGRAPHY.

1. Smith, F. M.: Experimental Observations on the Atypical *QRS* Waves of the Electrocardiogram of the Dog, Arch. Int. Med., 1920, **26**, 205.

2. Smith, F. M.: Further Observations on Experimental Lesions of the Branches of the Auriculoventricular Bundle of the Dog. In press.

3. Willius, F. A.: Arborization Block, Arch. Int. Med., 1919, **23**, 431.
4. Oppenheimer, B. S., and Rothschild, M. A.: Electrocardiographic Changes Associated with Myocardial Involvement, Jour. Am. Med. Assn., 1917, **69**, 429.
5. Herrick J. B.: Clinical Features of Sudden Obstruction of the Coronary Arteries, Jour. Am. Med. Assn., 1912, **59**, 2015.
6. Herrick, J. B.: Thrombosis of the Coronary Arteries, Jour. Am. Med. Assn., 1919, **72**, 387.
7. Wilson, F. N., and Herrmann, G. R.: Bundle Branch Block and Arborization Block, Arch. Int. Med., 1920, **26**, 153.
8. Wilson, F. N., and Herrmann, G. R.: An Experimental Study of Incomplete Bundle Branch Block and the Refractory Period of the Heart of the Dog, Heart, 1921, **8**, 229.
9. Lewis, T.: The Mechanism and Graphic Registration of the Heart-beat, New York and London, 1920, pp. 117–127.
10. Eppinger and Stoerk: Quoted from Wilson and Herrmann.
11. Cohn, A. E., and Lewis, T.: A Description of a Case of Complete Heart-block, Including the Postmortem Examination, Heart, 1912–1913, **4**, 15.
12. Cohn, A. E., and Lewis, T.: The Pathology of Bundle Branch Lesions of the Heart, Proc. New York Path. Soc., 1914, **14**, 207.
13. Krumbhaar, E. B.: Adams-Stokes Syndrome with Complete Heart-block without Destruction of the Bundle of His, Arch. Int. Med., 1916, **5**, 583.
14. Price, F. W., and Mackenzie, J. W.: Auricular Fibrillation and Heart-block in Diphtheria, Heart, 1911–1912, **3**, 233.
15. Pepper, W., and Austin, J. H.: Adams-Stokes Syndrome with Complete Heart-block and Practically Normal Bundle of His, Am. Jour. Med. Sc., 1912, **143**, 716.
16. Hume, W. E.: A Case of Heart-block in Which There Was No Pathologic Lesion of the Connecting Muscular System, Heart, 1913, **5**, 149.
17. Oppenheimer, B. S., and Pardee, H. E. B.: Site of the Cardiac Lesion in Two Instances of Intraventricular Heart-block. Read before the American Society of Clinical Investigation, Atlantic City, May 3, 1920.

POST-TRAUMATIC CALCIFICATION OF THE PANCREAS, WITH DIABETES.

By H. Gideon Wells, M.D.,
Chicago.

(From the Department of Pathology, University of Chicago, and the Otho S. A. Sprague, Memorial Institute.)

The condition described in the above caption is, as far as some search through the literature seems to indicate, altogether unique, and hence a case illustrating it is herewith reported in some detail, especially since evidence bearing on the relation of the pancreas to diabetes is also of value.

The subject was a man, aged thirty-two years, a teamster, who while driving his wagon fell from the seat. As to whether the wheels of the wagon passed over his body or not the evidence of bystanders was conflicting, but from the nature of the injuries found at the autopsy there can be no doubt that they did. This happened on March 31, 1919, and he was at once taken to the Cook County Hospital. The examination on his admission showed him

to be under the influence of alcohol, with the left sixth, seventh, eighth and ninth ribs fractured in the axillary line and considerable subcutaneous emphysema. No other injuries could be found, and, as far as the records show, no urinalysis was made. There was elicited a history of a fracture of an arm two years previously and of habitual alcoholism, but no evidence of any illnesses. He remained in the hospital until April 12, when he was discharged as recovered from the fractured ribs.

August 17, he was brought back to the hospital in an irrational, slightly stuporous condition, much emaciated and evidently seriously ill. It was learned that shortly after his return home a suppuration appeared on the inner side of the right elbow, which had not been observed to be injured while in the hospital, and from this there had been continuously a slight discharge of pus. His relatives stated that he had not been normal mentally since the accident, and he had been unable to work; he was irritable, stupid and made mistakes in conversation and in action. There was a progressive and marked loss of weight, estimated at about twenty pounds, although he had been slender previously. For three weeks previous to his return to the hospital he had been having typical attacks of Jacksonian epilepsy, increasing progressively in frequency and severity. The onset of each attack was with a sensation of stiffening in the left foot, followed by twitching and jerking which spread up the left thigh to involve the abdominal and chest muscles, then extended to the right lower extremity, then both upper extremities, beyond which the patient has no recollection. Sometimes the attacks were at intervals of not over one-half hour.

Observed in an attack in the hospital the patient began by having clonic spasms of the left lower extremity, then he stiffened his trunk and his arms began to jerk, his hands half closed, the fingers extended and shook; his mouth was half-open, his lower jaw moving in jerks, his facial muscles twitched and his eyes rolled. At the beginning of one of these spasms the patient gave successive loud cries. The spasms continued for about one or two minutes, and then the patient relaxed in about fifteen to thirty seconds; he was almost immediately conscious after the jerking stopped. There was no previous history of scalp injury, except being hit with a beer bottle about five or six years before; the blow dazed him for ten to fifteen minutes.

The only other information obtained was that he had had a slight cough for about a year and that he had had gonorrhea but not syphilis. On entering the hospital he complained of weakness, loss of appetite, nausea and great thirst. His relatives stated that for some time after his accident he had been noted to be extremely thirsty, drinking large quantities of water. Also he had complained of itching.

Urine had been passed during the convulsions, and so no estimate of polyuria was obtainable.

The chief physical findings on readmission to the hospital were the following:

The patient is a white man of about thirty-two years of age, of medium height, emaciated and in a slightly stuporous condition. There is a thickening of the end of the humerus at the internal condyle, with a slight stiffness of the elbow. A sinus opens about 4 cm. above the lower portion of the internal condyle, discharging a small amount of seropurulent fluid.

Teeth. Carious.

Tonsils. Moderately enlarged; rest of head negative.

Neck. Negative.

Chest. Symmetric and emaciated; clavicles prominent. The semistuporous condition of the patient makes it difficult to obtain findings. Rales present over the whole chest, specially the lower lobes.

Heart. Apex not palpable. Left border ½ cm. from midline, right border substernal. Rate, 128. First sound weak, second pulmonic accentuated. No murmurs.

Abdomen. Retracted and tense. Liver dulness, sixth interspace to costal margin. Kidney and spleen not palpable. No masses or tender spots.

Genitalia. Negative.

Extremities. Negative except for right elbow as mentioned. Reflexes exaggerated on left side. Some spasticity on left side.

Clinical Diagnosis. Chronic osteomyelitis of the right lower third of the humerus. Jacksonian epilepsy of undetermined etiology.

During the forty-eight hours that the patient was in the hospital he had repeated convulsions, during which urine was passed, and as there were no special indications of urinary change, no effort was made to secure specimens, so we have no record of the composition of the urine. The Jacksonian epilepsy dominated the picture completely, and he died in *status epilepticus* on August 20, and an autopsy was performed eight hours after death.

The autopsy findings were as follows:

External Appearance. The body is that of a small, poorly built, poorly nourished white man. *Rigor mortis* in legs and fingers. No edema. No icterus. No adhesions between the scalp and the skull. No evidence of trauma to head. Superficial lymph glands not enlarged. External genitals normal. No subcutaneous fat. On the inner aspect of the right elbow there is an elliptical opening in the skin, 10 by 20 mm., with a granulating floor, and the skin is much undermined. When cut through there is a superficial suppurating area between the skin and the muscle fascia anterior to the internal condyle, extending down into the internal condyle, where there is a suppurating cavity 1 cm. in diameter.

Abdominal Cavity. The inguinal and femoral rings are closed. Omentum is free from fat and adherent about the cecum. There are small hard lymph glands in these adhesions. The appendix lies behind the cecum and is remarkedly kinked on itself, forming a T, and is bound down by adhesions. There are also numerous vascular tags of adhesions over the sigmoid and elsewhere on the intestines. The mesenteric lymph glands are all slightly enlarged, pale and hard. The surface of the bladder is covered by a vascular connective tissue. There are numerous folds and bands of adhesions throughout the pelvis. The omentum is black from pseudomelanosis. There are dense fibrous adhesions about the spleen. There are also a few adhesions about the gall-bladder, elsewhere the liver is free. The peripancreatic glands are slightly enlarged. The retroperitoneal glands are normal in size.

Pleural Cavity. The left pleural cavity is partly obliterated, laterally and over the base, by dense fibrous adhesions. The right pleural cavity is completely obliterated. When the sternum was removed small pockets of pus were seen between the diaphragm and the lower margin of the right lung and chest wall. There is a hard white lymph gland present in the anterior mediastinum 1 cm. in diameter. Healed fractures of the sixth and seventh ribs can be felt on the left side at the anterior axillary line, with some overriding of the ends. Here the pleural adhesions are most dense. The lymph glands about the hilum of the left lung show small suppurating areas. There are numerous (twenty to thirty) small pockets of thick greenish-yellow pus lying beneath the parietal pleura on the right side, irregularly placed all over the cavity, in size up to 2 cm. in diameter. There are also a few such cavities within the pleural adhesions, specially between the diaphragm and the chest wall. No abscesses are found outside of the chest cavity or on the left side. There are no old fractures or other evidence of trauma on the right side. No subdiaphragmatic lesions.

Pericardial Cavity. Contains normal amount of fluid. There are protruding hyperemic areas showing through the left lateral aspect of the pericardium over the subpleural abscesses. The lining is smooth and not involved by this process.

Heart. Slightly enlarged. The left ventricle takes up the greatest area. There are small beaded areas in the coronary arteries. The right and left posterior cusps of the aortic valves are fused to each other by a soft fibrinous adhesion. The beginning of the aorta is nearly free from sclerosis. There is very little sclerosis in the thoracic aorta. Ductus arteriosus is closed. The tricuspid and mitral orifices are of normal size. The tricuspid and pulmonic valve cusps are normal. Along the free margin of the mitral valve, throughout its circumference, is a fresh growth of recent soft vegetations 1 to 3 mm. thick. Foramen ovale is closed. The walls of the ventricles are of normal thickness. The left

ventricle is stopped in diastole. The myocardium is slightly mottled in appearance; there are no definite macroscopic changes. The empty heart weighs 300 gm.,

Trachea. Normal.

Peribronchial Lymph Glands. No caseation or calcification; some contain small suppurating foci.

Esophagus. Normal.

Lungs. The left lung is inelastic and there are no definite areas of consolidation; weight, 600 gm. The lower lobe is very dark in color and contains much fluid. Every bronchus when cut is filled with creamy pus. The upper lobe shows the same condition, particularly in the posterior portion, less marked anteriorly. The right lung is covered with adhesions. Weight, 840 gm. There are some hard scars in the apex, especially the posterior part. Abscesses as described above are noticed in the pleural adhesions. There are also some small areas of hemorrhage in the pleura. Section through the upper lobe shows a distinct cavity 18 to 20 mm., running from which are lines of scar tissue. There is a caseous nodule at the upper apex 10 by 12 mm. Another small cavity is found in this upper lobe. There are some small gray tubercles in the peribronchial lymph gland that receives the drainage from the right upper lobe. There are no other definite areas of consolidation.

Spleen. Embedded in adhesions. Weight, 70 gm. The upper pole alone remains. The lower pole is hard, yellow, shrunken and covered with adhesions. When cut the entire lower pole is found to be replaced by a well-defined encapsulated necrotic mass, 5 x 4 x 3 cm. The rest of the spleen is very soft and pulpy.

Kidneys. The left kidney is surrounded by a mass of flabby fibrofatty tissue which is very adherent to the kidney. There is a total infarction of the left kidney. The size of the left kidney is approximately $5\frac{1}{2}$ x 4 x $1\frac{1}{2}$ cm. The structures are left in recognizable form but yellow and completely necrotic, without suppuration. The left renal artery is much smaller than the right and completely obliterated at the hilum of the kidney. Right kidney large, weight, 200 gm., soft. Cut surface shows cortical markings distinct. Cortex thick, 8 to 10 mm. There are no signs of abscesses. The capsule strips readily leaving a smooth surface.

Adrenals. Right adrenal seems normal in size and appearance. Left adrenal is normal except for one island of white tissue (5 x 10 mm.) in the medulla.

Liver. Dark in color and soft. Weight, 1900 gm. The cut surface shows considerable blood. The center of the lobules are dark. The cut surface is very wet. No other changes. Gallbladder: Normal. No concretions.

Pancreas. More rounded and thin than normal. Weight, 122 gm. The irregularity increases from head to tail. Head is distended with a mass the size of a hen's egg. Upon palpation the entire pancreas is full of small hard lumps, feeling as if filled with small stones. These concretions can be felt throughout the pancreas, about equally in all parts. They are all embedded in the tissue and a watery purulent fluid exudes from the ducts. They are not loose in the duct but are in the tissue itself, mostly firmly adherent; a few protrude into the duct, apparently by erosion from the outside. There are areas of partial stenosis along the pancreatic duct, but it is not anywhere completely obstructed. A few small concretions are found free in the duct. The entire pancreas is composed of scar tissue and calcified masses, no normal gland tissue being found. There is an increase in the peripancreatic fibrous tissues, but no concretions are found outside the gland tissue.

Stomach. Postmortem digestion. No lesion. Intestines: Normal.

Urinary Bladder. Greatly thickened with some hypertrophy of trabeculæ. Mucosa normal. *A small quantity of wine was present which contained* 2½ per cent *of sugar.*

Prostate. Somewhat enlarged and forms a ring about the urethra. There are no other gross changes. Seminal vesicles normal.

Testicles. Both normal.

Skull. The calvarium is normal. The dura on the external surface appears normal. There is no undue tenseness. There is a considerable amount of cerebrospinal fluid both between the dura and pia arachnoid and in the pia arachnoid. This fluid is clear.

Brain. Weight, 1500 gm. There is a diffuse reddish discoloration of the pia over the right lateral aspect, particularly at the junction of the frontal and parietal lobes. Elsewhere the pia is clear. There is an area of softening 4½ cm. long by 2 x 2½ cm. wide, involving the ascending frontal and ascending parietal convolutions in this area, the upper margin of the softening being 3 cm. from the midline. There is no evidence of suppuration in the meninges. The softened area averages 5 to 10 mm. thick, involving the gray matter chiefly. The lateral ventricles are of normal size, containing a clear fluid. The basal ganglia appear normal.

Anatomical Diagnosis. Infarction with softening of the right ascending frontal and parietal convolutions. Multiple subpleural tuberculous abscesses in the right chest wall. Bilateral hypostatic congestion and acute suppurative bronchitis. Bilateral adhesive fibrous pleuritis. Acute terminal mitral and aortic endocarditis. Complete anemic necrosis of the left kidney with compensatory hypertrophy of the right kidney. Healed anemic necrosis of lower three-quarters of the spleen. Extensive fibrosis and calcification of the entire pancreas. Pancreatic diabetes (glycosuria).

Healed fractures of the sixth and seventh left ribs. Abscess in internal condyle of right humerus with fistulous cutaneous opening. Parenchymatous degeneration of the liver and the right kidney. Hypertrophy of the urinary bladder wall. Healed appendicitis. Ulcerative and fibroplastic tuberculosis of the right pulmonary apex. Suppurative tuberculous mediastinal lymphadenitis. Hyperplastic tuberculosis of the mesenteric lymph glands. Healed necrotic area in the left adrenal. Healed diffuse peritonitis.

Histological Examination. *Pancreas.* The pancreas shows an extreme grade of fibrotic pancreatitis. (See Figure.) A small

Traumatic pancreatitis. This was one of the few islands of pancreatic tissue still present, located near the duct in the head of the pancreas. As will be observed, it consists chiefly of duct-like tubules rather than secretory structures, and these are isolated and compressed by scar tissue. Magnified 45 diam.

number of isolated, shrunken pancreatic islets remain, many being partially fibrosed. Besides these there are only traces of pancreatic tissue, although occasionally necrotic remains of pancreatic gland cells are found, barely recognizable. There are innumerable areas of calcification throughout the organ, each surrounded by dense fibrous tissue. The amount of replacement by fibrous tissue is so great that it is impossible to determine whether the calcific deposits are exclusively intra-alveolar or not, but certainly most of the calcium is deposited in the sites of necrotic glandular masses. Besides the large calcified masses the tissue is sprinkled everywhere with minute quantities of calcium salts, replacing small

groups of dead epithelial cells. No calcification of the vessels or of the fibrous septa is observed. Occasional islands of fatty areolar tissue remain within the fibrous masses, but these are never found calcified. No blood pigment is found.

Among the few small foci of recognizable glandular tissue that remain are many that consist of cells that have lost their nuclear staining and are surrounded by very heavy masses of fibrous tissue. A little pancreatic tissue that seemed capable of functioning is seen in only a few of the several parts of the gland that were examined, chiefly about the ducts near the head of the pancreas. These consist of the remains of lobules, with a dense fibrous capsule about them, fibrous tissue infiltrating between the atrophic tubules and ducts that remain, and occasionally a small atrophic Langerhans islet is recognizable. Nowhere is any area of even approximately normal pancreatic tissue to be found. It would seem that over 95 per cent, and probably fully 99 per cent, of the secreting pancreatic tissue has been replaced by fibrous tissue and calcium salts. There are no evidences of inflammation present, either tuberculous or acute.

Heart. The valves show recent vegetations. The myocardium is normal.

Lungs. The lungs show both old encapsulated and active tuberculosis, as well as acute hypostatic pneumonia and acute bronchitis.

Lymph Glands. The glands, particularly the intrathoracic glands, exhibit caseous and encapsulated tuberculosis, often with softening. The mesenteric and retroperitoneal glands show small tubercles, with much endothelial hyperplasia.

Adrenals. The left adrenal gland exhibits an extensive fibrotic area at the center, containing considerable blood pigment, apparently representing the site of a healed traumatic lesion. Elsewhere the adrenals are normal.

Liver. Shows no changes.

Kidneys. The right kidney shows a distinct increase in the size of the glomerules and tubules, without other noteworthy changes. The left kidney is completely necrotic, without sign of infection. Much thickening of the pericapsular tissues. The original structures are all visible but totally unstained.

Brain. Shows an old infarct with abundant blood pigment in phagocytes. The absorption of the necrosed tissue seems to be complete.

Spleen. The necrotic portion resembles a typical old infarct, with abundance of blood pigment, both granular and crystalline. The remaining living portion shows large Malpighian bodies and some blood pigment in the pulp.

Chemical Analysis of the Pancreatic Tissue. Samples from several parts of the alcohol-fixed gland were selected, to give a fair average

of the composition, and the inorganic material determined. In 0.9546 gm. of dried material was 0.6100 mg. of inorganic residue, or 63.9 per cent.

Several of the calcified masses were picked out of the pancreas and separated as completely as possible from tissue elements. They were analyzed for me by Miss Mary E. Maver, using the wet method used in my previous work on calcification, which method avoids the errors introduced by ashing.[1] Two such lots were analyzed at different times, and the following results were obtained:

PANCREATIC CALCIFICATION.

	Sample I.		Sample II.		
	Gm.	Percentage of inorganic.	Gm.	Percentage of inorganic.	Average per cent.
Ca	0.3765	35.6	0.1110	38.9	37.25
Mg	0.0028	0.27	0.0028	0.9	0.63
CO_2	0.2725	25.9	0.0696	24.2	25.05
P	0.0141	1.33	0.0008	0.27	0.80

Theoretically the inorganic elements existed as follows:

$CaCO_3$	0.8848	92.7	0.2738	95.20	93.95
$Ca_3(PO_4)_2$	0.0585	6.1	0.0040	1.39	3.74
$MgCO_3$	.....	.....	0.0098	3.4	
$Mg_3(PO_4)_2$	0.0103	1.08			

From these figures it is seen that the concretions consisted chiefly of calcium carbonate with but small quantities of calcium phosphate and magnesium salts. About 20 per cent of the calcium found could not be balanced with acid radicals. Search was made for oxalic acid and fatty acids, with which the calcium might have been united, but neither was obtained. It is observed that the analysis of two different lots agreed quite closely as far as the CO_2 was concerned, so it was certain that there was no loss in this determination. Thorough extraction with boiling amyl alcohol failed to dissolve out any calcium soaps. No silicate was present, a point of some interest, since some German writers have laid stress on the function of the pancreas as a storehouse for silicates and as a center of silicic acid metabolism.

This high proportion of calcium carbonate is entirely different from the figures usually obtained in analysis of calcified tissues, in which generally about 85 per cent of the inorganic material is calcium phosphate and about 10 per cent is calcium carbonate.

[1] Wells: Jour. Med. Res., 1906, **14**, 491.

On the other hand our figures agree closely with some of the figures given for calculi found in the pancreatic *ducts*. Thus, Möckel,[1] in his compilation on pancreatic calculi, gives the following figures reported in the literature: I, $CaCO_3$, 91.65 per cent (Johnston, Moynihan). II, $CaCO_3$, 82.0; $Ca_3(PO_4)_2$, 12.7 per cent (Maurice, Lussac). III, $CaCO_3$, 93.14 per cent; P_2O_5, 2.45 per cent (Lægrand, Scheunert). Other analyses of pancreatic calculi, however, have shown the chief constituent to be calcium phosphate. Presumably the predominance of calcium carbonate in pancreatic calculi, as well as in this one specimen of calcification of the pancreatic tissue, depends on the fact that the pancreas secretes a fluid alkaline with carbonates, since we find that the salivary duct calculi also sometimes consist chiefly of calcium carbonate, although these also may at times contain chiefly calcium phosphate.[2]

Discussion. The history and the autopsy findings establish this as a case of post-traumatic calcification of the pancreas with diabetes. The fractured left ribs, the traumatic infarction of the left adrenal, the left kidney and the upper pole of the spleen indicate that the changes of the pancreas were also the result of traumatism to the left side and the upper abdomen. Probably the wheel of the wagon went across the lower chest and the upper abdomen, since merely a fall from this height could scarcely have produced this amount of injury in these deep-seated organs. The history of great thirst, pruritus and progressive emaciation after the accident, together with the presence of sugar in the urine and the very extensive destruction of the pancreas, establish the diagnosis of traumatic pancreatic diabetes. The acute tuberculous changes in the pleura and lymph glands may be the result of the diabetes, although it is impossible to determine that they may not have been incited by the trauma in a subject with an existing pulmonary tuberculosis. Also, it is not certain whether the area of cerebral softening that caused the Jacksonian epilepsy was the result of the fall or had come from embolism; the histology of the brain lesion, however, suggests that it was contemporaneous with the lesions in the spleen, kidney and adrenal, and the history stated that the patient had never been normal mentally after the accident. The endocarditis was distinctly a terminal infection and too recent to have caused the lesions in the kidney, spleen, adrenal and brain.

The calcification seems to be distinctly of the pancreatic glandular tissue itself and is not the result of pancreatic fat necrosis, for not only were there no calcified foci in the fat tissue outside the pancreas, but even the fat tissue within the pancreas itself showed no calcification.

It is unfortunate that the patient was not brought into the

[2] Roberg: Ann. Surg., 1904, **39**, 669.

hospital until he was in a dying condition, and hence we have no data on the urine and the changes in the intestinal digestion that had resulted from so extensive a destruction of the pancreas.

Discussion of the Literature. As stated, no similar case can be found recorded. The extensive discussion of pancreatic cysts and concretions by P. Lazarus[3] makes no mention of calcification of the pancreatic tissue from any cause whatever nor of the occurrence of pancreatic calculi following trauma. He describes several cases in which scars and cysts have followed traumatism, but does not speak of calcification in connection with these. He also states that up to that time (1904) no case of diabetes had been described as a sequel of a traumatic cyst of the pancreas. Of interest in connection with our case is his statement that the most common cause of pancreatic trauma is being run over by vehicles and that the injuries are seldom of the pancreas alone, the liver, kidneys and spleen being often traumatized, as well as the ribs and the vertebral column. He also calls attention to the fact that only a part of the traumatisms of the pancreas are followed by fat necrosis, indicating that some added factor, such as infection or inflammation, must be present to produce this complication.

Opie in his monograph on *Diseases of the Pancreas* makes no mention of calcification of pancreatic tissues, nor does Kauffmann in his *Text-book of Pathologic Anatomy*. Numerous articles on pancreatic concretions have been reviwed, but in none of them do we find mention of calcification of the pancreas itself, except the statement in the article by Weichselbaum and Stangl[4] on the pancreas in diabetes that "in one case we demonstrated calcium deposits in the hyaline or sclerotic islands, whereby an increased similarity is given to sclerotic renal glomeruli." Neither is trauma mentioned as a cause of pancreatic calculus formation.[5]

While a complete search of all the literature on diabetes for cases of diabetes following trauma to the pancreas has not been possible because of the magnitude of the task a large number of articles and monographs have been reviewed, including practically all of the larger publications, virtually without finding any mention whatever of pancreatic trauma as a possible cause of diabetes. This is not strange in view of the fact that the pancreas is so well protected that only the most violent traumatism can injure it, and then the results are usually quickly fatal; if not fatal there is probably usually sufficient pancreatic tissue left to prevent diabetes. For example, Robeson and Cammidge in their work on the pancreas state that Garré was able to collect but 30 cases of pancreatic trauma, of which 3 recovered. Naunyn does not mention the possibility of diabetes as a result of trauma to the pancreas,

[3] Zeit. klin. Med., 1904, **51** and **52**.
[4] Wien. klin. Wchnschr., 1902, **15**, 972.
[5] Literature given by Möckel, Frankfurter Zeit. f. Pathol., 1920, **24**, 78.

but comments on the infrequency of diabetes following acute pancreatitis. Even the work devoted specifically to surgical diseases and injuries of the pancreas by Körte[6] makes no mention of calcification of the pancreas or post-traumatic diabetes. So, too, the works of von Noorden and Lépine are silent on this subject; the latter does mention traumatic diabetes as if depending entirely on nervous lesions, yet of 145 cases of traumatic diabetes collected by him in 8 the trauma is said to have been abdominal. Arnstein[7] in an elaborate review of 437 articles on chronic pancreatitis does not even mention either traumatic pancreatitis or calcification of the pancreas.

Jeanselme[8] reported, in 1897, 2 cases of bronzed diabetes, one of which, in a man aged forty-three years, was observed first a short time after receiving a blow near the umbilicus. The exact interval between the injury and the appearance of the symptoms of diabetes (marked thirst, anorexia, polyuria and loss of strength) is not given. It could not have been more than a few days, however, since it is said that the blow was received "at the beginning of the month of July," and the symptoms were said to have appeared about the 16th to 18th of the same month. Furthermore, nothing is said about the condition of the patient in the intervening time. Autopsy was performed on the fourth of the following January and disclosed the classic features of bronzed diabetes. The pancreas weighed 150 gm. and was irregularly pigmented. Microscopically it was sclerotic, although some lobules were little altered. Nothing was said in the autopsy report about the presence of any evidences of trauma in the abdominal cavity or elsewhere. With these scanty data it is not possible to prove that in this case the diabetes was the result of the abdominal traumatism, and it is highly doubtful that a traumatism to the pancreas could cause a bronzed diabetes in view of the evidence that in this disease the pancreatic sclerosis is the result of deposition of pigment in the pancreas.

In his work on the traumatic origin of internal diseases, Richard Stern[9] comments on the fact that in no published case of injury to the pancreas has glycosuria been observed.

We have found but one probably authentic case of post-traumatic pancreatic diabetes reported in the literature, by Grund.[10] The patient, a woman, aged twenty-five years, while six months pregnant, slipped on the ice and another person fell across her abdomen. After a period of abdominal pains and vomiting all symptoms subsided and a healthy child was delivered at term. A

[6] Die Chirurgischen Krankheiten und die Verletzungen der Pankreas, Stuttgart, W. Körte, 1898.

[7] Centrl. f. d. Grenzgeb. d. Med. u. Chir., 1912, **15**, 90.

[8] Bull. et mém. de la Soc. méd. des Hôp. de Paris, 1897, 3d series, **14**, 179.

[9] Ueber traumatische Entstehung inner. Krankheiten, Jena, 1913, 2d ed.

[10] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1907, **17**, 395.

month later pain and vomiting recurred with icterus, there being intervals of good health, with the gradual development of mild diabetes. About a year after the trauma a pancreatic cyst was operated on. The icterus subsided at once and permanently, but the diabetes persisted and within a few months assumed a comparatively severe form. The metabolic findings are tabulated as recorded during the various phases of the case; they show that the functions of the pancreas in respect to the digestive processes were not essentially altered. At the time of the publication of this report the patient was still living, and so we lack anatomic proof of the pathologic changes present.

The only instance of calcification of the pancreas tissue itself of which we can find record, beyond the apparently trivial involvement mentioned by Weichselbaum and Stangl, has been reported by Bernhard Fischer,[11] who states that it is, as far as he knows, a condition never previously described. The subject was a youth, aged eighteen years, with a striking family history of diabetic relatives, who had typical juvenile diabetes terminating in coma. There was no history of any trauma mentioned. The autopsy disclosed nothing of significance outside the pancreas, which was of normal size (100 gm.) and color, somewhat indurated, and showing macroscopically on the cut surface numerous tiny white calcific points, compared to the calcified glomerules in senile kidneys. Microscopically the changes were remarkable, for not only were the number and size of the islands of Langerhans enormously increased, but most of them showed calcification, often extensive, as well as sclerosis and hyaline degeneration. Some of the islands were so enlarged as to resemble adenomas, one of them being 1.3 mm. in diameter, and the number was so great that there must certainly have been a new formation of islands. The calcium salts stained with silver nitrate, and hence were presumably phosphatic, at least in part. Fine droplets of fat were sometimes found in the calcified islands. The connective tissue was considerably increased throughout the pancreas, but the glandular parenchyma was little altered. There was some calcification in the internal elastic lamina and the inner layers of the media of the arteries, but none in the parenchyma or stroma of the pancreas outside the islands. There was nothing found to explain why this remarkable selective calcification of the islands had occurred. Presumably they had undergone hyaline degeneration and then this hyaline material had become calcified as hyaline deposits everywhere are prone to do, perhaps because of a physical affinity for calcium salts.

Of course in pancreatic fat necrosis the freed fatty acids unite with calcium to form soaps, which might perhaps become converted

[11] Frankfurter Ztschr. f. Path., 1915, **17**, 218.

into phosphate and carbonate, although my own experiments indicate that the lesions of fat necrosis may disappear entirely within a short time,[12] and that implanted soaps are mostly reabsorbed rather than replaced by the less soluble phosphate and carbonate.[13]

Summary. A previously healthy young man fell from a wagon and was probably run over by at least one of the wheels. He received fractures of several ribs on the left side, traumatic infarction of the left adrenal, the upper pole of the spleen and the entire left kidney, together with a crushing injury of the pancreas, which resulted in almost complete destruction of the secreting elements, which were replaced by a large quantity of dense fibrous tissue and extensive deposits of calcium salts. Analysis showed that about 64 per cent of the dry weight of the pancreas consisted of inorganic salts, chiefly calcium carbonate. Jacksonian epilepsy developed, the result of necrosis of a considerable area of the cerebral cortex, presumably occurring at the same time as the other injuries. The patient became rapidly emaciated, exhibited great thirst and the urine found in the bladder at autopsy contained sugar. A review of the literature has failed to reveal a similar case of extensive pancreatic calcification, whether post-traumatic or otherwise, or an analogous case of diabetes following crushing injury of the pancreas.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGIC POINT OF VIEW*

By John A. Fordyce, M.D., Isadore Rosen, M.D.,

and

C. N. Myers, Ph.D.,

New York.

(From the Department of Dermatology and Syphilology, and the Department of Biologic Chemistry, College of Physicians and Surgeons, Columbia University, New York.)

PART I. ANALYTICAL METHODS.

Clinical medicine has for a long time felt the necessity of correlating its work with the biologic laboratory where definite chemical reactions and tests are employed to reveal the end-results of body function. During the past decade biologic chemistry has advanced with enormous strides and has yielded invaluable aid to the clinician, as the study of blood chemistry alone will show. Syphilis therapy, too, owes in a large measure its success to this branch of medicine,

[12] Jour. Med. Research, 1903, **9**, 70. [13] Ibid., 1907, **17**, 15.

* Received for publication, February 2, 1922.

for the progress made in the treatment of this disease with the newer arsenicals would have been impossible without the experimental research carried on in animals.

Since the introduction of arsphenamin into the realm of therapeutics many questions have been in debate, especially those concerning the amount of arsenic in the body fluids, or, more specifically, the blood and spinal fluid. Through the courtesy of Prof. Gies, of the department of biologic chemistry, College of Physicians and Surgeons, who has been kind enough to aid us in our undertaking, we have carried on a series of studies during the past two years. Originally it was our intention to examine about 100 specimens to determine (*a*) the amount of arsenic found in the blood at different intervals after intravenous injections of arsphenamin, and (*b*) whether arsenic is present in the spinal fluid after intravenous medication. As the work progressed new problems presented themselves which required the study of other phases of this subject and led to our analyzing about 2000 specimens.

Owing to the lack of hospital facilities we were able to investigate only the urine, blood and spinal fluid. These being the most important fluids of the body, we hope the data obtained will be of value in deciding a number of debatable questions.

In our work we have taken into consideration the fact that there is probably a decided variation in the amounts of arsenic found in these fluids, the dosage being the same, in individuals of different age, weight, sex and state of health. This will be discussed in detail in a paper which will appear later. The important question whether arsenic finds its way into the spinal fluid will be considered not only from a theoretic standpoint but from the results of numerous examinations of spinal fluids from patients treated intravenously.

Our studies, which will appear in several instalments, include the following problems:

1. When is the largest amount of arsenic found in the blood after an intravenous injection?
2. Is there a difference in the arsenic content of the blood serum and the clot?
3. When is the largest amount of arsenic found in the urine?
4. What is the variation in the amount of arsenic found in the blood and the urine at the same intervals?
5. Does the use of normal saline in the preparation of the solution exert any influence on the amount of arsenic demonstrable in the blood and urine?
6. Is the arsenic content in the blood and urine related to the stage of the disease? Is there any differences in these fluids from early, late, latent and Wassermann-fast cases as well as non-syphilitic patients?
7. What is the quantity of arsenic present in the blood and

urine at varying intervals after intramuscular injections of neoarsphenamin?

8. Does the amount of arsenic in the blood and urine vary according to the preparation employed, namely, arsphenamin, neoarsphenamin and silver arsphenamin?

9. Can arsenic be demonstrated in the blood and urine months after the cessation of treatment?

10. (*a*) Do patients who develop arsphenamin jaundice show an excess of arsenic in the blood and urine?

(*b*) Can arsenic be demonstrated in these patients at longer intervals after the cessation of treatment than in non-jaundiced cases?

11. (*a*) Is arsenic demonstrable in the spinal fluid after intravenous injection?

(*b*) Can it be found in all cases or in only a certain percentage?

12. When after an intravenous injection is the largest amount of arsenic found in the spinal fluid?

13. Is the quantity increased when intensive intravenous treatment is employed, *i. e.*, daily injections for three doses?

14. Does the amount of arsenic present in the spinal fluid vary with the preparation used, *i. e.*, arsphenamin, neoarsphenamin or silver arsphenamin?

15. Does the type of neurosyphilis play a role in the quantity of arsenic present in the spinal fluid?

16. Does intraspinal treatment influence the amount of arsenic found in the spinal fluid at future examinations?

17. Is there any relationship between the strength of the Wassermann reaction of the spinal fluid and the amount of arsenic present?

18. Does a relationship exist between the type of colloidal gold reaction and the amount of arsenic found?

19. Is there a relationship between the amount of globulin found in the spinal fluid and the quantity of arsenic present?

20. In what quantities is arsenic present in the milk of treated nursing syphilitic mothers?

The fact that arsenic, by whatever channel absorbed, causes tissue changes (and the symptoms resulting therefrom fairly warrant the inference that it enters into chemical reaction with the constituents of those tissues) and if it disappears therefrom sooner than it does from the liver and other parenchymatous organs it is because the form of combination is less stable in the one case as compared with the former. Upon this basis the use of arsenicals rests upon distinct physical, chemical and dynamic fundamentals as applied to the therapeutic treatment of disease. Based upon the above conception, it immediately becomes evident that an active and an inactive variety of arsenic should exist in that the amount that is eliminated so rapidly had little or no opportunity to produce any sterilizing effects and that the amount left is so small that it may be a cause for many Wassermann-fast cases.

As early as 1839 arsenic was detected in the blood drawn from the veins of the human subject in life, whereas Seidel (1882) reported that arsenic is found in the corpuscles but not in the plasma. In the light of our present knowledge slightly different views are held.

In a succeeding paper absorption, elimination, retention and the normal values will be discussed for the reason that each of these subjects needs considerable elaboration. It is quite necessary to make a few of these preliminary remarks that it may be clear that the subject arsenic is not new, that the methods of elimination are being rediscovered, that the analytic procedures are not unusual or novel.

The opening paragraphs very aptly point out the problems which may be elucidated by the application of a large variety of procedures which have not been utilized with uniformity together with accurate clinical study.

Elimination of arsenic begins very early and takes place during the progress of its absorption. Elimination takes place through the urine, the feces, the epidermic tissues and to some extent by perspiration, the breath, milk and menstrual blood (Segale, 1904).

With these possibilities of elimination it is immediately apparent that only the more accessible modes of elimination can be studied, and, furthermore, the amount *retained* is the part of essential interest.

The systematic removal of arsenic from other extraneous material, both organic and inorganic, has been the subject of much study for more than a century. These systematic contributions have offered many modifications, and it may now be said that quantitatively accurate methods are available for determining minute quantities of the element.

Generally speaking the analyst thinks of three methods for determining arsenic toxicologically or for use in medical jurisprudence where delicacy and accuracy are involved. These methods are generally spoken of as the Reinsch, Marsh and Gutzeit tests. These three methods will be briefly spoken of later. In addition the method of Schneider and Fyfe (sometimes spoken of as the method of Liebig-Ludwig), based upon the separation of the arsenic as the trichloride in the presence of ferrous chloride, has been utilized. It is a distillation method, and it is hardly reliable in estimating minute quantities of arsenic. The distillate of arsenic trichloride is then introduced into the Marsh apparatus.

The methods of Gautier (1875) and of Chittenden and Donaldson (1880) are highly commendable when the suggestions of Lockemann are carefully applied. The original methods are unreliable if the oxidation proceeds too violently, with consequent loss of arsenic.

The Neumann (1897) method is based on the same principle as the Gautier method, from which it differs in that the nitric acid

is generated in the mixture, which renders the process more easily manageable.

The method of Igefsky and Nikitin (1900) uses sulphuric acid alone for the destruction of organic material. The Strzyzowski method (1907) destroys the organic matter in the presence of magnesium or calcium oxide, which retains the arsenic during the process of incineration. The Fresenius and von Babo method is well adapted to the systematic search for minerals in general. It utilizes the oxidizing properties of potassium chlorate.

The Reinsch test is valuable when an abundance of material is available. It may be applied directly to a liquid containing organic matter, such as urine, and may be completed in a few minutes. It is based upon the use of copper foil, whereby a stain is produced by the arsenic. The method is applicable in certain cases and in others modification is necessary. Most hydrochloric acid contains small amounts of arsenic. Copper likewise is frequently contaminated with arsenic. Arsenates should be reduced to arsenites with sulphur dioxide and the excess gas expelled. The practical limit of delicacy of this test is placed at 0.0065 mgm. Wormley (1877) claims a delicacy of 0.00065 mgm. The general consensus of opinion is that the method is inferior to the Marsh test.

The Gutzeit test is capable of considerable accuracy provided the organic matter is properly destroyed. However, the question of reagents is one that requires considerable attention. The most disturbing feature of the test is found in selecting paper of the proper absorbing power to be used in selecting standards. The amount of mercury salt absorbed due to variations in thickness of the paper, the lack of uniformity of paper, the degree of moisture in the paper, together with the reagents, have led the authors of this series of articles to adopt the Marsh-Berzelius method. The Gutzeit method is regarded as second to the Marsh method in delicacy and accuracy in determining small amounts of arsenic.

The Marsh test is the most delicate and reliable of the tests for arsenic. Nothing of the original process as described by Marsh remains in the present method of application except the fundamental principles—generation of arsin and its decomposition by heat. Zinc and sulphuric acid or electrolytic hydrogen may be used in liberating the nascent hydrogen used in the process. Electrolytically a regular flow of gas is obtained as long as the current remains uniform. No zinc is required by this procedure. It is to be recommended where there is electric installation. However, the other method—zinc and sulphuric acid—is just as reliable if care and caution are exercised in the selection of the reagents.

In 1914, Myers studied the application of the Marsh method to the determination of arsenic in cerebrospinal fluid following the administration of neosalvarsan (see Barbat, 1915). In order to

place the elimination and retention of arsenic on a more scientific basis it has been apparent that more detail and extensive application have been necessary. To study the chemotherapeutic action of our present-day arsenicals the *frequency of the dose, the stage of the disease, the presence or absence of other complicating pathologic conditions are factors which will determine the conclusions that may be drawn.* The human organism is a vast biologic experiment, and conclusions from an experiment of this kind must be drawn with conservatism resulting from applications to a large number of individuals, thereby eliminating certain idiosyncrasies which at first glance do not become apparent. The study of the elimination of 1 case or even 2 cases would be quite absurd on account of the biologic error which results from diet, disease and amount of liquid used by a patient.

To carry out the investigations and answer the questions which are proposed at the beginning of this paper, it has been necessary as well as wise to review a great deal of the literature. Time and space are not available to point out many of the valuable suggestions that have been useful in carrying out this extensive piece of work. This investigation has been in progress for two years, and in its entirety about two thousand analyses are already involved. The bibliography which is attached will give the casual reader references sufficient to gain a comprehensive idea of the entire subject.

As the result of extensive investigation the Gutzeit and the Marsh-Berzelius methods are found to be most reliable. Preference is expressed in favor of the Marsh modification in that it is believed to be more sensitive in combination with a sufficiently higher degree of accuracy. Myers (1918) described briefly the technic employed. In the present article it has seemed wise to go into details so that any investigator can duplicate these results with the use of average skill and precaution in its application to clinical methods.

Apparatus. This laboratory has decided to treat all determinations on the dry basis for the reason that variation in the specific gravity of the specimens—due either to pathologic conditions or abnormalities—has been so large that it was not reliable to depend on volume or weight volume figures. With this view in mind it is desirable to select an analytic balance of a type similar to the one illustrated in Fig. 1, having a guaranteed accuracy of 0.1 mg. A set of weights of corresponding accuracy is desirable.

Porcelain casseroles, analytic balance, analytic weights, specimen tubes, desiccator with calcium chloride, steam water-bath, drying oven, platinum dish, beakers, funnels, filter stand, filter paper, graduated glass-stoppered cylinders (100 cc) and Marsh apparatus are required to carry out these determinations.

Reagents Required. All reagents are chemically-pure and free of arsenic. Concentrated nitric acid, concentrated sulphuric acid (special arsenic-free), ferric ammonium sulphate, sodium nitrate, potassium nitrate, standard solution of arsenious oxide, ammonium hydroxide, lead acetate paper, anhydrous calcium chloride (granular), absorbent cotton and distilled water.

All reagents should be examined by the user. Experience has shown that nothing can be taken for granted, and it is on this basis that the present investigation is carried out. When the reagents are found satisfactory it is advisable to order the entire stock of material which is to be used throughout the entire investigation. The arsphenamin products

FIG. 1.—Analytical balance with accuracy of 0.1 mg.

used in these experiments are identical in arsenic content, trypanocidal activity and source of manufacture, so that all variations of every kind, with the exception of those due to analytic errors or those involved in the biologic economy are eliminated.

Porcelain casseroles of good quality serve as a convenient type of container. They are heavy enough that the breakage is small. During the present investigation two out of thirty sets have been broken. They are also remarkably constant in weight. The 50 and 100 cc capacity are found most satisfactory for the type of specimens examined. The number used will be determined largely by the extent of the work and the rapidity of carrying out the determinations. These dishes should be dried to constant

weight in an air oven and stored in a desiccator, as illustrated in Fig. 2, ready for use. The weight of the specimen is accurately obtained by difference.

Royal Berlin porcelain casseroles were found most satisfactory as far as breakage and constancy of weight are concerned. The sizes used in these investigations are known as No. 2 and No. 3.

The dishes and their contents after weighing are placed upon the steam-bath and dried. The containers are then dried in the air oven to constant weight.

FIG. 2.—Section of hood capable of accommodating 70 digestions at one time. Desiccator contains dried specimens at the right. Casseroles on water-bath contain specimens. Air oven at left used for drying specimens to constant weight.

When this procedure is finished the organic material is destroyed by using a mixture of nitric and sulphuric acid, then by means of sodium and potassium nitrate, and finally by fusion at low temperature in the platinum dish. The details will be found under Procedure.

The reagents are all tested by means of the control method and the Marsh method.

Preparation of Reagents. The special arsenic-free nitric and sulphuric acids are used in preparing this acid mixture. The acid is prepared by mixing 900 cc of concentrated nitric acid and 100 cc of concentrated sulphuric acid. A large supply of these acids is obtained in the beginning, so that there are no variations due to composition of the reagent.

The solution which is to furnish the iron for absorbing the arsenic is prepared so that each cubic centimeter of solution contains approximately 50 mg. of ferric hydroxide. If 226 gm. of *ferric* ammonium sulphate are dissolved in water and made up to 1 liter a solution satisfactory for this purpose will be obtained.

The concentrated arsenic-free sulphuric acid is diluted, so that the resulting solution contains about 25 per cent of the concentrated acid. Experience has shown that this concentration gives a very satisfactory evolution of hydrogen.

One of the important factors is the careful preparation of the standard arsenic solution which is used in making the standard mirrors illustrated in Fig. 5. A tenth normal solution of arsenic trioxide is used as a starting-point. It contains 4.95 gm. of arsenic trioxide per liter and should be carefully standardized by any of the well-known volumetric or gravimetric procedures. The correction factor must be accurately known, that is, the solution may be a trifle weak, or *vice versa*. This solution is carefully diluted, using volumetric flasks of known calibration, so that each cubic centimeter of solution will contain metallic arsenic equivalent to 0.000001 gm. In other words, if 1, 2, 3, etc., cc of this diluted solution are used the resulting mirrors will contain 0.000001, 0.000002, 0.000003 gm. of metallic arsenic. Sometimes these values are expressed as so many parts per million. In these articles the values are expressed in milligrams of metallic arsenic per 100 gm. of dried specimen.

In order to avoid loss of time in preparing the standard arsenious acid solution the method of preparing it and standardizing it is given in detail together with the principle involved.

"The solution of alkaline arsenite is prepared by dissolving 4.95 gm. of the purest sublimed arsenious oxide in about 250 cc of distilled water in a flask with about 20 gm. of pure sodium carbonate. It is necessary that the acid should be in powder, and the mixture needs warming and shaking for some time in order to complete the solution; when this is accomplished the mixture is diluted somewhat, cooled, then made up to the liter.

"In order to test this solution, 20 cc are put into a beaker with a little starch indicator and the iodin solution allowed to flow in from a burette, graduated in 0.1 cc, until the blue color appears. If exactly 20 cc are required the solution is strictly decinormal; if otherwise the necessary factor must be found for converting it to that strength.

"The principle upon which this method of analysis is based is the fact that when arsenious acid is brought in contact with iodin in the presence of water and free alkali it is converted into arsenic acid, the reaction being:

$$AS_2O_3 + 4I + 2K_2O = As_2O_5 + 4KI.$$

"The alkali must be in sufficient quantity to combine with the hydriodic acid set free, and it is necessary that it should exist in the state of bicarbonate, as caustic or monocarbonated alkalies interfere with the color of the blue iodide of starch used as indicator.

"If, therefore, a solution of arsenious acid containing starch is

titrated with a solution of iodin in the presence of an alkaline bicarbonate the blue color does not occur until all the arsenious acid is oxidized into arsenic acid. In like manner a standard solution of arsenious acid may be used for the estimation of iodin or other bodies which possess the power of oxidizing it."

Sodium and potassium nitrate solution is prepared by using equal parts of the dry salt and then making a saturated solution.

Dry sodium and potassium nitrate are mixed in equal parts and then ground up to a fine powder in a mortar.

It is quite important at this point to call attention to the fact that this entire investigation has been carried out in a laboratory free from arsenic contamination. All reagents, containers, etc., are new and utilized exclusively for these refined experiments. Manufacturing, laboratory and arsenic treatment rooms are in entirely different buildings.

Control Experiments. In order to test the efficacy of the method involving the destruction of the organic matter and the subsequent deposition of the arsenic in the capillary tubes it is necessary to carry out these parallel experiments.

First, it is necessary to establish the purity of the zinc and the sulphuric acid in relation to their possible content of arsenic. Through the courtesy of the New Jersey Zinc Company, Palmerton, Pa., a satisfactory grade of arsenic-free zinc is available. Analyses show that it contains 0.0000002 gm. of arsenic in 100 gm. of zinc. The amount of zinc consumed in an analysis varied between 5 and 10 gm., so that the amount of arsenic in the zinc is very small and is negligible as far as this method is concerned.

Through the coöperation of the J. T. Baker Chemical Company, Phillipsburg, N. J., special arsenic-free sulphuric acid is available. This is diluted so that the solution contains about 1 part of the concentrated acid and 3 parts of water.

The homemade Marsh apparatus consists of a well-made bottle of 300 to 500 cc capacity. Into this bottle a tightly fitting two-hole rubber stopper fits. A 250 cc dropping funnel is used to slowly admit the solution. It is advisable to draw the end of the funnel to a capillary so that the intake of fluid can be easily controlled. The bent tube fits tightly into the other opening of the stopper. In every instance be sure that all connections are tight. About one inch from the lower opening of the exit tube there is a small opening used as a trap to prevent vapors being mechanically carried over into the drying bulbs. In the bend of the tube and in the first bulb, lead acetate paper, cut in strips, is placed for the purpose of absorbing any hydrogen sulphide that may be liberated. The remaining bulbs are loosely filled with granular anhydrous calcium chloride to sufficiently dry the liberated gases. At the end of the tube a small plug of absorbent cotton is placed for the purpose of preventing explosions in case the gas is lighted too soon

before all the air is expelled. By means of a clean rubber connection a piece of Jena hard-glass combustion tubing is attached. This tubing is drawn out to a capillary and all other pieces should be made similarly and of uniform diameter. The portion of the tubing which is to be heated to cherry redness is surrounded by a piece of nichrome gauze, fitting very closely for the following reasons: (*a*) The heat is distributed around the entire tube; (*b*) if the pressure of the gas becomes too great the tube while near its melting-point will not blow out. In order to concentrate the heat, pieces of thin asbestos board are placed at each end of the heated area and one above. Heat is obtained from a Meker burner or two well-regulated Bunsen flames.

In order to deposit the metallic arsenic in a definite area a cool stream of water is allowed to slowly flow over the tube as illustrated in Fig. 4. Cold water or iced water is placed in the second dropping funnel and allowed to flow slowly by capillarity over the capillary tube. In this manner the arsenic is collected in a uniform manner and can be easily compared with standard known amounts.

Precaution. In solutions contaminated with H_2S, H_2Se, H_2T, H_3P, H_3Sb, S, zinc sulphide will produce a grayish-white deposit at the place where the arsenic mirror should appear. In carrying out analysis, proper consideration for these possibilities should always be taken into account. Allow the hydrogen to flow for several minutes and then light the gas flowing from the end of the capillary tube. If the light persists and shows no tendency to strike back it is safe to light the larger flames. If this precaution is not observed explosions may follow, much to the danger of other workers, to say nothing about the analyst. Replace the solution in the bottle after each determination. Under ordinary circumstances the lead acetate and the calcium chloride will do for several determinations. A new piece of Jena tubing is necessary for each determination. These tubes can be drawn out several times and then the short pieces may be sealed together, making the expense for tubing a small factor.

Fifty grams of zinc are placed in the bottle of the Marsh apparatus illustrated in Fig. 4 and 100 cc of concentrated sulphuric acid diluted, as described under Reagents, are allowed to act upon the zinc with the evolution of hydrogen. The acid is allowed to drop into the bottle slowly. If any arsenic is present it will be hydrogenated and decomposed as it passes through the heated portion of the glass tube. After decomposition the metallic arsenic will be deposited on the cold portion of the tube. The evolution of gas is allowed to continue over a period of several hours, and if no mirror is formed the acid and zinc are considered satisfactory and free from arsenic in the sense that it contains an amount less than the limits of accuracy of the method. The hydrogen gas

should flow at a uniform rate—at most, not too fast to lead to the formation of hydrogen sulphide. This is decomposed in the hot portion of the tube and leads to the deposition of a sulphur film.

A few drops of copper sulphate or platinic chloride will hasten the evolution of hydrogen in case a delayed reaction takes place when the acid is added to the zinc.

Jena hard-glass combustion tubing, about 7 mm. in diameter, is the only tubing which has given satisfactory results. Pyrex tubing has either shown a deposit or turned brown at the place where the mirror is to be formed. Any tubing will be suitable

FIG. 3.—Battery of arsenic adsorptions and filtrations just after the specimen has been fused. Twenty or thirty filtrations and adsorptions are carried out simultaneously.

provided it will stand high temperatures, will show no darkening when heated and will give no deposit just beyond the point of heating.

If the evolution of hydrogen is too rapid there will be an escape of arsin which has a garlic-like odor. The arsin is passing through the heated tube so rapidly that it is not decomposed. Amounts of arsin as small as 1 part in 10,000,000 can be detected by its odor.

By this scheme the purity of the sulphuric acid and the zinc is fully established. The next step consists in using the nitrate salts in the same manner as described under Procedure. The solution

is then treated with the iron solution, precipitated with ammonium hydroxide, washed and redissolved. This solution is then run through the Marsh apparatus. The purity of all the reagents will be well established and only one final step remains before the comparisons are made.

In order to test the control method it is necessary to make experiments which are very similar to those by which we examine the blood and other fluids in question: 20 cc portions of normal guinea-pig blood are obtained and placed in porcelain casseroles; 6 of these samples are used in the following manner: Sample No. 1 is used exactly as it has been obtained from the animal while the remaining four samples are added to solutions containing 1, 3, 5, 7 and 10 parts, respectively, per 1,000,000 of arsenic. In this manner we have a blank experiment and five solutions containing different amounts of arsenic. At least four sets of these experiments were carried out in order to test the method which was to be used. By carrying out these experiments the method is carefully checked as far as the possibility of loss is concerned. In parallel with these experiments the standard arsenic solution is Marshed and the results compared with those which have gone through the entire process of destruction of organic material.

TABLE I.

Cubic centimeter standard arsenic solution used.	Mirror in parts per 1,000,000 found.	Cubic centimeter standard arsenic solution used with guinea-pig blood.	Mirror in parts per 1,000,000 found.
Blank.	Blank.	Blank.	Blank.
1	1		
2	2		
3	3	3	3+
4	4		
5	5	5	5
6	6		
7	7	7	7
8	8		
9	9		
10	10	10	10−

By repeating this comparison with and without blood it was found that the method checked up very well. The standard mirrors were prepared by using 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 cc of the standard arsenic solution. The Marshing process must be carried on slowly, so that there is no loss of arsenic in the form of arsin.

Specimens. In this investigation, urine, blood-clot, serum, spinal fluid, milk, etc., are collected in sterile tubes and placed in the ice-box until used. In no case should decomposition be allowed to take place for the reason that loss of arsenic may result. It has been shown conclusively that microörganisms may cause the liberation of volatile arsenic compounds. Huss (1913) studied 90 organisms and found that 10 of these liberated ethyl arsin. Several

of these types were not identified, but among them were: Penicillium brevicaule, Aspergillus caudidus, Aspergillus clavatus as well as some actinomyces.

Witthaus (1911), page 583, describes the organisms which may liberate arsenic as follows:

"Gosio found that common moulds growing in the presence of arsenic compounds evolve a volatile substance containing arsenic and having a pronounced garlic-like odor. The action of Penicillium brevicaule was found to be more pronounced in this regard than that of other moulds, and Gosio has based upon it a test for the presence of arsenic which is claimed by some to be more delicate than the chemical tests. Many other moulds, however, behave similarly, *e. g.*, Mucor mucedo, Penicillium glaucum, Aspergillus vivens, etc., and Schmidt has given a list of thirteen varieties of mould which are active in this manner when grown upon sour paste. The discoveries of Gosio have been verified by Abba, Sanger, Morpurgo and Brunner, Schmidt, Baumert, Bode, Abel and Buttenberg, Scholtz and Maasen."

In other words, the specimens were examined under the most favorable circumstances. Every analysis has a distinct clinical history connected with it, thereby giving an accurate correlation of chemical, clinical and serological findings under controlled conditions.

The specimens were all dried under standard conditions, total solids estimated and arsenic determinations made as described under procedure.

Procedure. The specimen is carefully transferred and weighed in a porcelain casserole of suitable capacity. The specimen is then dried at low temperature, preferably on a water-bath. It is then dried in the air oven to constant weight. At least 5 cc of spinal fluid, blood and serum should be used, and 25 cc of urine and larger quantities of the other fluids.

The dried specimens are now treated with mixed acid, drop by drop. A rapid addition of acid may cause foaming, spattering and charring, accompanied by a loss of arsenic. If there is no vigorous reaction the casserole and its contents are placed on the water-bath and allowed to digest. If much oil or fat is present the contents may creep up on the side of the dish. Digestion is continued until the specimen has a yellow oily-like appearance. Practice has indicated that the following amounts of acid usually digest the following specimens:

Mixed acid in cc.	Specimen.
5	Spinal fluid
7	Serum
15	Blood
30	Clot
15	Urine

In case the specimen is not properly digested an additional amount of acid is required. To this yellow oily mass a saturated solution of the nitrate mixture is added, an amount equivalent to 15 gm. of the dried salts. Further digestion is carried on until a crystalline mass is obtained by further evaporation on the water-bath. This process continues the oxidation and also provides alkali salts which combine with the arsenic present. This crystalline mass still contains traces of organic matter which is destroyed by fusing 10 gm. of the dry mixed salts in a platinum dish at the lowest temperature possible. The yellow crystalline mass is added

FIG. 4.—Shows Marsh apparatus set up in battery formation. Graduates at the right of each apparatus used to make the volume up to 100 cc. Graduated in cubic centimeters. Each operation handles 6 outfits simultaneously.

slowly to this fused mass by means of a spatula. The whole mass is then fused at a higher temperature with the escape of the nitrous fumes. The porcelain casserole is heated and washed out with 5 cc of concentrated sulphuric acid. When the fused mass has cooled the sulphuric acid is added to the platinum dish and heated gently. There will be a further evolution of nitrous fumes. The fused mass is then dissolved in water and boiled. The contents of the platinum dish are then washed into a beaker of about 300 cc capacity. To this solution the ferric ammonium sulphate is added in amounts corresponding to those in the table. The acid is then partly neutralized. The precipitate of ferric hydroxide

should never be made while the solution is even warm. It must always be done in the cold. The precipitated ferric hydroxide adsorbs the arsenic quantitatively as shown by several authors referred to in the bibliography. The iron-arsenic precipitate is filtered off as illustrated in Fig. 3. The second adsorption is carried out by the addition of more ferric ammonium sulphate to the filtrate, precipitated by ammonium hydroxide and filtered in the same funnel. A third adsorption is carried out in a similar manner by using the second filtrate. The amounts of ferric ammonium sulphate in cubic centimeters used in the three adsorptions for the following specimens are shown below:

Adsorption.	Spinal fluid.	Blood or clot and serum.	Urine.
1	10 cc	15 cc	20 cc
2	5 cc	15 cc	15 cc
3	3 cc	10 cc	10 cc

When all the precipitate has been collected in the funnels the precipitates are washed with distilled water until they are free of nitrates. (Use the ferrous sulphate test on a sample acidulated with sulphuric acid.) After careful washing the iron precipitate is dissolved in 5 cc of concentrated sulphuric acid and made up to 100 cc in graduates shown in the plate with the Marsh apparatus. These solutions will keep indefinitely or until the Marsh test is carried out.

When the Marsh apparatus is working smoothly and the Jena tube is heated to redness the whole solution or an aliquot is allowed to flow in slowly—one drop in every three to five seconds. It is necessary to see that a continuous evolution of hydrogen is maintained.

As a rule it requires about thirty minutes for each Marsh test. In specimens in which considerable arsenic may be suspected it is advisable to use only 5 cc of the solution with 25 cc of water, so that a slow rate of flow will be maintained. If a mirror is obtained with this amount the experiment is completed, otherwise continue adding the solution from the cylinder until a mirror is obtained or the specimen is proved to be arsenic-free.

Quantities as small as one-half part per 1,000,000 are readily detected. The lower range of the scale should be utilized in so far as it is possible. The final calculations are made on the basis of 100 gm. of natural and dry material. The arsenic is expressed in milligrams of metallic arsenic and also in percentage.

In carrying out these experiments, conditions and arrangements are made so that every process is going along simultaneously with those involved with the entire work. All details are given with the intention of carrying out analysis on a large scale.

Fig. 5 shows the range of standard mirrors ranging from the blank to 10 parts per 1,000,000. It is impossible to use this illus-

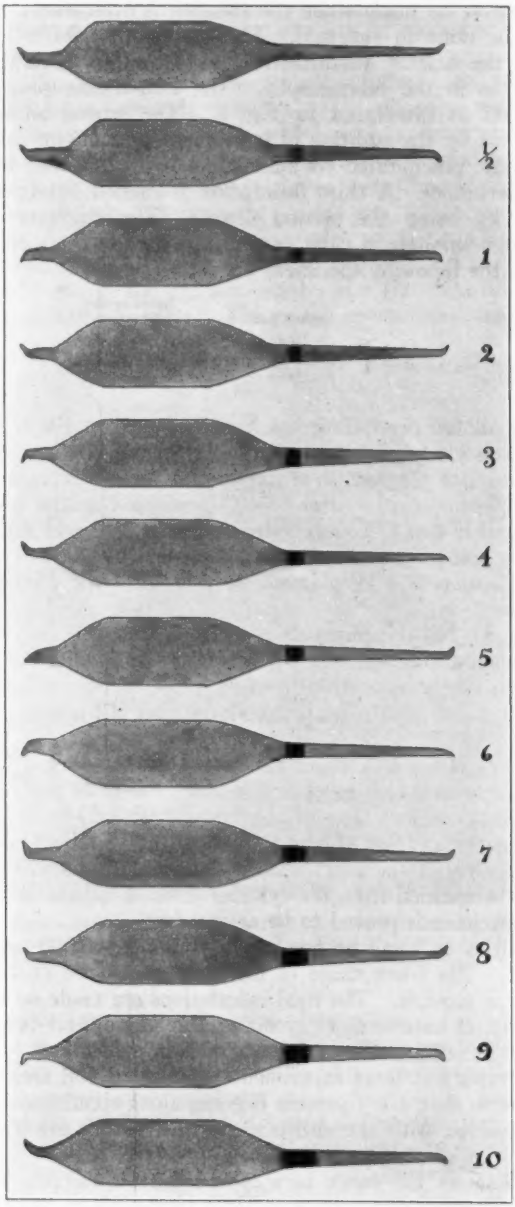


FIG. 5.—Each part indicated in the numerals at the right represents 0.001 mg. of arsenic.

tration for actual comparison in the analytic procedure for the reason that the luster and glass effects must be taken into account. Fig. 5 shows the gradations of readings with very good accuracy. The figures at the right represent parts per 1,000,000, or expressed in milligrams the values are 0.001 mg., etc., when the readings are 1, 2, etc.

The succeeding papers will give detailed information regarding the relation between the clinical and analytic data found.

BIBLIOGRAPHY.

Aarken, Aaron, and Corper, H. J.: 1916. The Tuberculocidal Action of Arsenic Compounds and Their Distribution in the Tuberculous Organism, Jour. Infect. Dis., **18,** 335.

Abelin, J.: 1911. Ueber eine neue Methode das Salvarsan nachzuweisen, München. med. Wchnschr., **58,** 1002. Beginn und Dauer der Ausscheidung Salvarsans durch den Urin nach intravenoeser Injektion, München. med. Wchnschr., **58,** 1771.

Baecche, Brunetto: 1913. The Changes in the Biological Properties of the Blood Serum in Phosphorus and Arsenic Poisonings, Parma. Accad. sci. e littere Modena, through Ztschr. Immunitaet., 11 Teil, Ref. 5, p. 1168.

Bailey, Cameron V., and MacKay, Angus: 1920. Toxic Jaundice in Patients under Antisyphilitic Treatment. A Study of the Chemical Analyses of the Blood and Urine and Observations on the Effect of Exercise and Diet in the Treatment of Syphilis, Arch. Int. Med., **25,** 628.

Bang, Ivar: 1916. The Amount of Arsenic in Normal Urine, Allm. Sv. Lakaretidn., **13,** 549.

1917. Quantitative Determination of Arsenic in Urine, Farmacevisck Revy. Schweiz. Apoth. Ztg., **55,** 393.

Barbat, J. H.: 1915. Finding of Arsenic in Cerebrospinal Fluid Following Intravenous Administrations of Neosalvarsan, California State Jour. Med., No. 11, **13,** 415.

1918. Permeability of the Meninges to Arsenic in Paresis and Tabes, Jour. Am. Med. Assn., No. 3, **70,** 147. (See note on p. 148.)

Barthe, M.: 1907. Localization of Arsenic. Repert. pharm., No. 19, **3,** 497.

Beeson, Barker, B., and Albrecht, P. G.: 1922. The Elimination of Arsphenamin and Neoarsphenamin in the Urine. A Chemical and Clinical Study of the Abelin Reaction, Arch. Dermat. and Syph., **25,** 51.

Bergman, Hans: 1919. The Storage and Excretion of Arsenic after Administration as Salvarsan in Serum and Water, Biochem. Ztschr., **90,** 348.

Billeter, O.: 1919. Determination of Small Quantities of Arsenic, Hilvetica Chim. Acta., **1,** 475.

Bloemendal, W. H.: 1909. Arsenic in the Animal Organism, Arch. pharm., 246, 599.

Blumenthal, Ferdinand, and Navassart, Emanuel: 1911. Atoxyl Elimination and Distribution of Arsenic after Injection of Atoxyl and Derivatives, Biochem. Ztschr., **32,** 380.

Blyth, Alexander Wynter: Poisons; Their Effects and Detection, with an Introductory Essay on the Growth of Modern Toxicology. London: C. Griffin & Co.; New York: Wm. Wood & Co.

Bongrand, J. Charles: 1912. Elimination of Arsenic after Treatment with Organic Compounds of Arsenic, Bull. Soc. pharm., **18,** 152.

Bornstein, A.: 1911. Fate of Arsphenamin in the Body, Deutsch. med. Wchnschr., **37,** 112.

Boswell, Maitland C., and Dickson, J. V.: 1918. The Adsorption of Arsenious Acid by Ferric Hydroxide, Jour. Am. Chem. Soc., **40,** 1793.

Carles, P.: 1917. Arsenic in Sodium Sulphate, Med. Jour., Bordeaux, **88,** 300.

Carlson, C. E.: 1907. On the Different Behavior of Organic and Inorganic Arsenic Compounds toward Reagents and on Their Proof and Their Determination

in the Urine after Introduction into the Organism, Lund Ztschr. f. physiol. Chem., **49,** 410.

Chittenden, R. H., and Donaldson, H. H.: 1880. On the Detection and Determination of Arsenic in Organic Matter. I. Method for the Complete Extraction of Arsenic from Organic Matter, Am. Chem. Jour., **2,** 236.

Delepine, Sheridan: 1919. Report on Certain Organs in a Case of Fatal Poisoning by Arseniuretted Hydrogen Gas, Jour. Ind. Hyg., **1,** 356.

Dercum, F. X.: 1920. Functions of Cerebrospinal Fuid. Spinal Drainage and Intraspinal Injections of Arsphenaminized Serum, Arch. Neurol. and Psych., **3,** 230.

Desbourdeaux, Leon: 1920. The Determination of Arsenic and Phosphoric Acids in the Presence of Large Amounts of Salts, Bull. Soc. pharm., **27,** 225.

Duret, Paul: 1918. Investigation, Determination and Excretion of Arsenic in the Urine, Compt. rend. soc. biol., **81,** 736. A New Method for the Destruction of Organic Matter, Compt. rend. Soc. de biol., **167,** 129.

Eichhorst, H.: 1920. Changes in the Liver, Kidneys and Blood Due to Acute Arsenic Poisoning, Deutsch. Arch. f. klin. Med., No. 3 and 4, **131.**

Eichler: 1912. Severe Arsenic Poisoning after Salvarsan Infusion, München. med. Wchnschr., **59,** 2871.

Ekeley, J. B.: 1913. Distribution of Antemortem Administered Arsenic in Human Cadaver, Jour. Am. Chem. Soc., **5,** 483.

Escallon, J.: 1912. The Elimination of "606" in the Urine, Lyon méd., **119,** 377.

Evans, B. S.: 1920. A New Process for the Estimation of Arsenic, with Notes on the Chemistry of the Marsh-Berzelius Process, Analyst, **45,** 8.

Ewins, Arthur, J.: 1916. Estimation of Arsenic in Organic Compounds, Jour. Chem. Soc., **109,** 1355.

Fischer and Hoppe, J.: 1909. The Course of Organic Arsenic Preparations in the Human Body, München. med. Wchnschr., **56,** 1459.

Foulerton, Alexander, G. R.: 1920. On Poisoning by Arsenobenzol Compounds Used in the Treatment of Syphilis, British Med. Jour., No. 3104, p. 864.

Frankel-Heiden and Navassart, E.: 1913. The Fate of Salvarsan in the Human Body, Ztschr. f. exper. Path. u. Therap., **13,** 531.

Freymuth: 1916. Detection of Salvarsan in the Urine, Apoth. Ztg., **31,** 387.

Fuehner, H.: 1918. Simple Process for the Estimation of Small Quantities of Arsenic in Corpses, Berlin pharm. Ges., **28,** 221.

Fyfe, Andr.: 1852. Ueber die Auffindung des Arseniks, Jour. f. prakt. Chem., **55,** 103.

Gaebel, G. Otto: 1911. Salvarsan in Forensic Testing, Arch. Pharm., **249,** 49. Titration of Salvarsan with Iodine Solution, Arch. pharm., **249,** 241.

Ganassini, Domenico: 1920. Behavior in the Marsh Apparatus of Certain Organic Arsenic Compounds Used as Drugs, Boll. chim. farm., **58,** 285.

Garnier, L.: 1910. Arsenic in the Liver in Acute Poisoning, Compt. rend. Soc. de biol., **67,** 738.

Gautier, A.: 1875. Sur la recherche et dosage de l'arsenic contenu dans les matières animales, Bull. Soc. d. chim. de Paris, **24,** 250.

1899. The Normal Existence of Arsenic in Animals and its Localization in Certain Organs, Compt. rend., **129,** 929.

1920. Normal Arsenic in Living Tissues and Traces of Iodine Found in Air and in Water. Some Necessary Corrections, Compt. rend. Soc. de biol., **170,** 261.

Gautier, A., and Clausmann, P.: 1917. Destruction of Tissues for Detection of Arsenic and the Examination of the Ash, Compt. rend. Soc. de biol., **165,** 11.

Green, Henry H.: 1918. The Fate of Arsenic after Ingestion by, and Injection into, Live Stock and after Absorption through the Skin in Dipping, S. African Jour. Sci., **11,** 72. Note on the Microtitration of Arsenic, S. African Jour. Sci., **14,** 518.

Green, Henry H., and Dijkman, Cornelius Derksen: 1919. Some Experiments on the Fate of Arsenic in the Animal Body, S. African Jour. Sci., **15,** 640.

Greven, K.: 1910. The Commencement and Duration of the Excretion of Arsenic in the Urine Following Treatment with Ehrlich-Hata Dihydroxy-diaminoarsenobenzene, München. med. Wchnschr., **57,** 2084.

Gunn, James A.: 1908. The Action of Arsenic on the Red Blood Corpuscles and a Theory of the Blood Defect in Pernicious Anemia, British Med. Jour., No. 2481, p. 145.

Hall, George W.: 1915. Presence of Arsenic in the Spinal Fluid, Jour. Am. Med. Assn., **64,** 1384.

Hall, G. W., Callender, R. W., and Holmblad, E. C.: 1920. Presence of Arsenic in Spinal Fluid, Arch. Neurol. and Psych., **3,** 631.

Haller, David A.: 1917. The Treatment of Syphilis of the Central Nervous System. A Comparison of Mercurialized Serum and Salvarsanized Serum, Arch. Int. Med., **19,** 997.

Hamilton, G. R.: 1921. Arsenical Keratosis and Epithelioma, British Jour. Dermat. and Syph., **33,** 15.

Harkins, W. D., and Swain, R. E.: 1909. The Chronic Arsenical Poisoning of Herbivorous Animals, Jour. Am. Chem. Soc., **30,** 928.

Hartman, Willy: 1919. Arsenic. Ztschr. f. anal. Chem., **58,** 148.

Heffter, A.: 1915. The Deposition of Arsenic in the Hair, Vtjschr. ger. Med., **49,** 194.

Heiduschka, A., and Biechy, Th.: 1911. Determination of Arsenic in Urine after the Administration of Salvarsan, Apoth., Atg., **26,** 146.

Hodkin, F. W., and Turner, W. E. S.: 1920. The Discoloration Produced by Lead, Antimony and Arsenic in Lamp-worked Glass Tubing. Jour. Soc. Glass Tech., **4,** 158.

Holland, E. B.: 1916. Detection of Arsenic in Bees, Jour. Econ. Ent., **9,** 364.

Huss, Harold: 1913. Microörganisms Forming Arsin, Svensk Farm. Tidskrift, **17,** 265.

Igefsky and Nikitin: Quoted by Scherbatcheff, D., 1900. Ueber die Dauer der Ausscheidung des Arsens in gerichtlichchemischer Beziehung, Vrtljschr. ger. Med., 3 F. **19,** 243.

Irokawa, K.: 1914. Excretion of Arsenic in Urine after Subcutaneous or Intravenous Injection of Salvarsan, Sei-I-Kwai Med. Jour., **33,** No. 10.

Jeanselme, E.: 1914. Localization of Arsenic in the Viscera after Injection of Salvarsan, Presse méd., **21,** 857.

Joachimoglu, G.: 1917. The Form in which Arsenic and Arsenious Acids Are Excreted, Arch. f. exp. Path. u. Pharm., **80,** 317.

Jones, E. Gabriel: 1919. British Pharmacopeia Quantitative Limit Test for Arsenic, Analyst, **44,** 235.

Kirkby, William: 1918. Marsh's Apparatus, Pharm. Jour., **100,** 286.

Klason, Peter: 1914. Quantitative Determination of Arsenic in Organic Secretions and Compounds, Arkiv. Kemi. Min. Geol, No. 9, **5.**

1916. Estimation of Small Quantities of Arsenic, Arkiv. Kem. Min. Geol., No. 5, **6,** 1. Determination of Small Amounts of Arsenic and the Normal Content of Urine, Svensk. Kem. Tidskrift, **28,** 69; Arkiv. Kem. Min. Geol., **6,** 1.

Kling, Andre: 1917. Arsenical Dextrose, Ann. Falsif., **10,** 438.

Kobert, Rudolf: 1906. Lehrbuch der Intoxikationen, Stuttgart-Enke.

Koelsch, F.: 1920. Toxic Action of Arseniuretted Hydrogen, Zentralblatt f. Gewerbehygiene, **8,** 121.

Koetter, Karl: 1914. Investigations on the Excretion of Salvarsan in the Urine after the Intravenous Injection of Concentrated Aqueous and Concentrated Serum Solutions of Salvarsan. Observations on the Influence of Diuresis on the Excretion of Salvarsan, Med. Klin., **10,** 807.

Kohn-Abrest, E., and Bouligaud: 1917. Accidental Presence of Arsenic in Chemical Products and in Some Foods, Ann. chim. anal., **22,** 85, 107, 128, 1920. General Method for the Detection and Determination of Arsenic, Compt. rend. Soc. de. biol., **171,** 1179.

Kosian, Wilhelm: 1915. Method for the Determination of Arsenic in Urine, Blood, and Parts of Cadavers, Pharm. Post., **48,** 321.

Kunkel, A. J.: 1905. Beiträge zur Frage des sogenannten normalen Arseniks, Ztschr. f. physiol. Chem., **44,** 511.

Kyrle, Josef: 1914. Excretion of Arsenic in the Urine after a Single Subcutaneous Administration of Salvarsan, Vienna Med. Klin., 1914, p. 368; Zentr. Biochem. Biophys., **16,** 650.

Laignel-Lavastine: 1920. Arsenic in General Paralysis, La médecine, February, 1920.

Launoy, L.: 1918. Toxicity of Colloidal Arsenic and Arsenic Compounds, Compt. rend. Soc. de biol., **81,** 164.

Lehmann, F.: 1912. Estimation of Arsenic in Salvarsan and Neosalvarsan, Apoth.-Ztg., **27,** 545.

1913. Estimation. II. Examination of Blood and Urine, Arch. Pharm., **251,** 1.

Leredde and Rubinstein (see Leredde and Domaine): 1921. Traitement et prophylaxie de la syphilis, ed. 2, Paris, Maloine et Fils, Editors, p. 320.

Lewitt, M.: 1917. The Excretion of Salvarsan after Intravenous Injection of Concentrated Solutions, Deutsch. med. Wchnschr., **42,** 518.

Lillig, R.: 1920. Importance of the Occurrence of Arsenic in the Soil, in Plants, and in the Animal and Human Organism to the Forensic Chemist, Pharm. Ztg., **65**, 500.

Lockemann, George: 1911. Detection of Small Amounts of Arsenic in the Urine Blood, and Other Organic Materials, Biochem. Ztschr., **35**, 478. The Absorption of Arsenic by Iron Hydroxide, Pharm. Zentr., **51**, 1131.

1913. History of Marsh Test for Arsenic, Chem. Ztg., 36, 1465.

1916. Comparative Investigations on Arsenic Excretion in the Human Urine after Injection of Different Arsenicals (Atoxyl, Arsacetin, Arsenophenyglycin, Salvarsan, Neosalvarsan), Biochem. Ztschr., **78**, 1.

Luehrig, H.: 1909. Interesting Toxicological Cases, Pharm. Zentr., **50**, 534.

Maiye, M.: 1917. Examination of Urine of Syphilitic Patients Treated with Various Preparations of Japanese-made Salvarsan, Hifukwa, Hitsunyodwa Zasshi, **17**, 67; Jap. Med. Lit., **2**, 5.

Marshall, J., and Ruan, L. A.: 1909. Is Arsenic Given Off in Gaseous Combination When Putrefactive Changes Occur in Tissues Derived from Animals Poisoned with Arsenic, Univ. Penna. Med. Bull., **22**, 180.

McIntosh, J.: 1914. The Fixation of Arsenic by the Brain after Intravenous Injections of Salvarsan, Proc. Roy. Soc., London (B) **88**, 320.

McIntosh, J., and Fildes, P.: 1916. Factors which Govern the Penetration of Arsenic (Salvarsan) and Anilin Dyes into the Brain, Brain, **39**, 478.

McNally, William D.: 1917. Retention of Arsenic in the Organs, Jour. Am. Chem. Soc., **39**, 826.

Mees, R. A.: The Nails with Arsenical Polyneuritis.

Mehrtens, H. S., and McArthur, C. G.: 1919. Arsenic Penetration of the Meninges during the Treatment of Neurosyphilis, Proc. Soc. Exp. Biol. Med., **16**, 99.

Muto, K., and Sanno, Y.: 1912. The Elimination of Arsenic after the Intramuscular Injection of Dihydroxyaminoarsenobenzene, Therap. Monatsh., **25**, 599.

Myers, C. N.: 1916. Arsenic in "Chemically Pure" Zinc, U. S. Public Health Reports, **31**, No. 40, 2654.

1919. Determination and Distribution of Arsenic in Certain Body Fluids after the Injection of Arsenobenzene, Salvarsan, and Neosalvarsan, U. S. Public Health Reports, **34**, No. 24, 881.

Myers, C. N., and Du Mez, A. G.: 1918. Qualitative and Quantitative Tests for Arsphenamin and Neo-arsphenamin, U. S. Public Health Reports, **33**, 1003.

Neumann, A.: 1897. A Simple Method for the Determination of Phosphoric Acid in Metabolism Experiments, Arch. f. Anat. u. Physiol. Phys. Abth., p. 552.

New York Medical Journal: 1920. The History of Arsenic, **111**, 337.

Onaka, Marizo: 1911. The Action of Arsenic on the Red Blood Cells, Ztschr. f. physiol. Chem., **70**, 433.

Orfila, M.: 1838. Poisoning by Arsenious Acid, Bull. de l'Acad. de méd., Paris, **3**, 676.

Petren, K.: 1919. The Primary Toxicity of Neosalvarsan, Lancet, **197**, 244.

Pomaret, M.: 1920. Elimination of Arsphenamins, Medecine, No. 2, **2**, 123.

Rabow and Strzyzowski: 1908. Does Arsenic Pass into the Hair after Treatment with Atoxyl? Therap., Monatsh., **22**, 197.

Riebes, E.: 1914. The Absorption of Salvarsan and Neosalvarsan in the Organism, Arch. f. Derm. u. Syph., p. 118, Orig., p. 757.

Rieger, John B., and Solomon, Harry C.: 1919. Circulation of Arsenic in the Cerebrospinal Fluid, Jour. Am. Med. Assn., **71**, 15.

Rijn, W. van: 1919. Estimation of Small Quantities of Arsenic, Pharm. Weekblad, **56**, 1072.

Rogers, L. Joslyn: 1920. Determination of Arsenic in Organic Compounds such as Salvarsan, Can. Chem. Jour., **3**, p. 398.

Romijn, G.: 1917. Pharmacopeia Tests for Arsenic in Drugs, Pharm. Weekblad, **54**, 1216.

Rupp, E., and Lehmann, F.: 1911. A Simplified Determination of Arsenic in Atoxyl and Arsacetin, Apoth. Ztg., **26**, 203.

Ryan, Leon A.: 1915. Distribution of Arsenic in Liver Tissue in Cases of Poisoning, Jour. Am. Chem. Soc., **37**, 1959.

Salkowkie, E.: 1909. Arsenic in Urine, Ztschr. f. physiol. Chem., **56**, 95.

1916. The Nature of Excreted Arsenious and Arsenic Acids, Arch. f. exp. u. Path. Pharm., **80**, 231, 219.

Scheringa, K.: 1920. Determination of Small Amounts of Arsenic, Pharm. Weekblad, **57**, 420.

Schilling and Naumann: 1913. Distribution of Arsenic in the Animal Organism, Arch. Schiffs- u. Trop. Hyg., **16,** 101; Zentr. f. Biochem. u. Biophys., **13,** 125.

Schmidt, E.: 1917. Arsenic Trisulphide, Arch. Pharm., **255,** 45.

Schneider, Wien: 1852. Abscheidung des Arsens aus organischen Substanzen, Arch. Pharm., 2 R, **70,** 40.

Segale, M.: 1904. Determination of Arsenic in the Normal Tissues by Biological Methods, Ztschr. f. physiol. Chem., **42,** 175.

Sieburg, Ernest: 1916. Biology of Aromatic Arsenic Compounds, Ztschr. physiol. Chem., **97,** 53. Esters of Aromatic Arsenic Compounds of p-Arsenobenzoic Acid with Amino Acids and Higher Alcohols, Arch. d. Pharm., **254,** 224.

Sneed, M. C.: 1918. A New Method for the Separation of the Copper Group from the Arsenic Group, with Special Reference to the Identification of Arsenic, Jour. Am. Chem. Soc., **40,** 187.

Stern, Carl: 1918. The Excretion of Salvarsan after Intravenous Injection of Concentrated Solutions, Deutsch. med. Wchnschr., **42,** 416.

Strathy, George S., Smith, C. H. V., and Hannah, Beverley, M. B.: 1920. Delayed Arsenical Poisoning, Lancet, **198,** 802.

Strune, H.: 1908. The Detection of Arsenic by Means of the Marsh Apparatus, Ztschr. f. anal. Chem., **12,** 761.

Sutton, Francis: A Systematic Handbook of Volumetric Analysis, or The Quantitative Estimation of Chemical Substances by Measure Applied to Liquids, Solids, and Gases. P. Blakiston's Son & Co., Phila.

Terry, Robert W.: 1919. Arsenic. Midland Drug, **53,** 132.

Ullmann, Karl: Excretion and Retention of Arsphenamin, Arch. f. Dermat. u. Syph., **114,** 511.

Underhill, P.: 1915. Distribution of Arsenic in the Human Body, Jour. Biol. Chem., **19,** 513.

Underhill, Frank P., and Davis, Stanton H.: 1922. The Excretion of Arsenic after Serial Administration of Arsphenamin and Neo-arsphenamin, Arch. Derm. and Syph., **5,** 40.

Usuelli, P.: 1913. Elimination of Arsenic by Patients Treated with "606," Giorn. ital. malatt. vener., **53,** No. 2, Zentr. f. Biochem. u. Biophys., **14,** 382.

Utz: 1920. The Detection of Arsenic in Salvarsan and Neosalvarsan, Pharm. Zentralhalle, **61,** 39.

Venin: 1913. Treatment of Syphilis in the Army with Salvarsan and Related Substances, Proc. Thirteenth Intern. Med. Cong., 1913, Sect. 13, p. 176.

von Maschka, J.: 1881. Handbuch der gerichtlichen Medicine., **2,** 249; 4 vol., 8vo, Tübingen.

Vuaflart, L.: 1916. Detection of Arsenic by Means of Mercuric Chloride, Ann. Falsif., **9,** 446.

Warren, W. H.: 1915. Laboratory Manual for the Detection of Poisons and Powerful Drugs (translation, Autenrieth, W.), p. 167.

Wasicky, R., and Mayhofer, A.: 1918. Arsenious Acid. Pharm. Post., **51,** 409.

Webster, John: 1916. Excretion and Secretion of Salvarsan and Neosalvarsan, Analyst, **41,** 231.

Willcox, W. H., and Webster, John: 1916. The Toxicology of Salvarsan, British Med. Jour., No. 1, p. 474.

Wilson, L. A.: 1918. The Evaluation of Zinc Dust; a Proposed Method of Analysis, Chem. Met. Eng., **19,** 32.

Witthaus, Rudolph August: 1911. Manual of Toxicology, William Wood and Co., New York.

Wormley, Theodore G.: 1877. Fallacies of Reinsch's Test for Arsenic, Am. Jour. Med. Sci., **74,** 399.

Zimmermann, W.: 1921. Sensitive Test for the Hydrides of Arsenic, Antimony and Phosphorus by Means of Gold Chloride, Apoth.-Ztg., **36,** 26.

Zimmern, F.: 1913. Infusion or Injection of Arsphenamin, München. med. Wchnschr., **60,** 1087.

THE WASSERMANN REACTION IN NON-LUETIC CASES.

By T. McKean Downs, M.D.,
PHILADELPHIA.

(From the Undergraduate Medical Association, Medical School, University of Pennsylvania, and the Laboratories, Philadelphia General Hospital.)

On December 14, 1920, a young man, aged nineteen years, entered the medical wards of the Pennsylvania Hospital, service of Dr. George W. Norris, suffering from malaria, which he had contracted five months before on the coast of Mexico, while serving in the navy. He had been treated and supposedly cured, and was now suffering from a return of typical symptoms of tertian malaria. His previous medical history was negative. Up until five months previous he had never been ill enough to see a doctor, and he denied venereal history—never any sore on the genitals, no rash, sore-throat, falling of the hair, severe headaches or pains in his bones at any time. His family history was also entirely negative, father and mother living and well, and he never had heard that his mother had had miscarriages.

His physical examination was negative, except for the enlarged spleen characteristic of malaria, a slightly enlarged liver, and a marked pallor. His eyes and teeth were perfectly normal; there were but few palpable lymph nodes; supracondylar glands not felt; no periosteal nodes or bowing of the tibiæ; lungs clear; heart normal and genitalia negative.

His blood on admission showed red blood cells, 2,560,000; hemoglobin, 42 per cent, and was loaded with tertian parasites. Urine negative.

He was immediately put upon quinine, 30 gr. per day, and Blaud's pills, and at once began to improve.

On December 17, the laboratory reported that the patient's blood Wassermann was weakly positive. Spinal fluid was not examined. On December 21, the patient was discharged, with instructions to take quinin for ninety days, according to Bass's advice[1] and then return to have his Wassermann repeated.

This case caused much discussion as to the significance to be attached to his positive Wassermann. There was an impression among the staff that malaria is frequently associated with a positive reaction, but as no one was definitely sure of this the decision was reached to ignore the Wassermann and treat his malaria, taking up the question of syphilis later. I may say here that he has not appeared since and has been lost track of. Letters to his address are returned by the post-office.

[1] Bass, C. C.: Jour. Oklahoma Medical Association, 1920, **13**, 281.

The question thus raised was only partially settled by reference to certain widely used text-books. Osler's *Practice*, edition of 1920, failed to mention the possibility that the Wassermann might be positive in diseases other than syphilis. Schamberg, in his *Dermatology*, edition of 1915, says only "Positive Wassermann reactions may be obtained in yaws, and in a proportion of cases of malaria, leprosy, etc., and within a period of twenty-four to forty-eight hours after the administration of ether."

Osler and Churchman (*Modern Medicine*, 1914) say the reaction is positive in syphilis, tubercular leprosy and fresh malaria; that in other fevers and wasting diseases partial deviation of complement may occur, but these reactions are not truly positive.

Lespinasse[2] says the reaction is not absolutely specific but is considered evidence of syphilis except in yaws, tubercular leprosy, some cases of relapsing fever, malaria during the febrile stage, some cases of experimental trypanosomiasis and beriberi. In all other cases it is impossible to rule out associated syphilis.

Connor[3] says that false positives are known to occur in leprosy, yaws, relapsing fever, malaria during the febrile stage and in diabetes with acidosis.

When the Wassermann reaction was first introduced it was supposed to be specific—to be dependent upon a specific substance in the blood. Subsequent investigation has shown this belief to be fallacious; but though the theory of the test has been impugned, investigation has merely confirmed the belief in its specificity. Its efficiency is very high—all early luetic cases can be detected if several tests are done at short intervals, provided the technic is right. At the same time there have been many reports of cases other than syphilis with a positive reaction. Many of these reports can be accounted for by faulty technic. The test is so complicated, and such meticulous accuracy is required in all its details, that there is a large leeway for error and the human equation. By now the test as done in a good laboratory can be relied on and the results of different men on the same specimen of blood are in most cases consistent, but this degree of efficiency did not always obtain.

There is at present no standardized method generally accepted for conducting the test, and there are nearly as many modifications as there are workers in this field. The wonder therefore is that the test is so very reliable.

The antigens in most common use are the syphilitic, the Noguchi and the cholesterinized—the latter the most sensitive.

The reading of the test is important. The readings usually reported are four-plus, complete inhibition; three-plus, over 75 per cent inhibition; two-plus, 50-75 per cent inhibition; plus,

[2] Tice's Practice of Medicine, 1920.
[3] Oxford Loose-leaf Medicine, 1921.

25-50 per cent; plus-minus, under 25 per cent; and negative, complete hemolysis. In many cases only four instead of five positive degrees are reported.

These five or six reports may, for all practical purposes, be condensed into three—positive, complete inhibition of hemolysis; negative, complete hemolysis; and doubtful, anything between the two. A positive reaction means syphilis if the few other conditions that are still recognized as giving a positive can be excluded. One single negative standing alone is worthless in excluding lues, but is very valuable confirmatory evidence, and a doubtful reaction must be interpreted by the clinician. It is unjust to any patient to diagnose syphilis by the *Wassermann alone*, unless it shows complete or practically complete hemolysis. In a case known to be luetic, a doubtful (one, two or three plus) reaction is an indication for further treatment.[4]

It is the clinician's business to interpret the test; the laboratory should merely report the behavior of the serum when tested. For this reason Craig thinks it better that the laboratory man should not know the history of the case, lest his reading of the test be biassed and erroneous.

There is hardly a disease known in which the Wassermann has not at some time been reported positive, but most often in the other protozoan diseases. So striking used to be the proportion of positives in these cases, that R. Müller, of Vienna,[5] decided that scarlatina could not be a protozoan disease because he so rarely found the Wassermann positive, though he says positives do occur, rarely, in the disease. (I need not say that Müller stands practically alone in this view of the reasons for regarding scarlet fever as non-protozoal in etiology.)

Müller found that in 88 per cent of cases of yaws the Wassermann reaction is positive. He records that the results of different authors in malaria are variable. Bohn, he says, found a positive reaction in 35 per cent of his 46 cases, the reaction disappearing when the malaria was cured.

Bauermann and Wetter (quoted by Müller) using larger material, found only occasionally an incomplete reaction, almost exclusively as the fever was rising. A reaction still positive three days after the disappearance of all fever, in their opinion, signifies lues.

Other non-specific positives are rare. The reasons why they do occur are not known. Müller gives 3 per cent positive in advanced tuberculosis and says that the test is very occasionally positive in various tumors, especially carcinoma, but only when the patient is *in extremis*, with generalized metastases.

Tubercular leprosy shows the large proportion of 19 per cent

[4] See "The Wassermann Test," by C. F. Craig, 1921.
[5] Die Sero-Diagnosé der Syphilis, 1913, Vienna.

of positive reactions, but curiously enough, in Müller's experience, the anesthetic form was invariably negative.

Kolmer and Casselman[6] found the Wassermann to be weakly positive in 19 per cent of cases of psoriasis. Of 250 cases of scarlet fever they found none with a positive reaction.

They record 5 cases of malaria; 3 of these had negative reactions; of the other 2, 1 was frankly luetic. The history of the other patient was not obtained. In discussing this paper, Dr. John A. Roddy, of Philadelphia, said that in the Canal Zone, during the summer of 1913, he saw hundreds of cases of malaria on whose serum a Wassermann reaction was performed, with uniformly negative results.

Kolmer[7] says the reaction is highly specific, but is so beset with technical difficulties that much confusion has been caused. Many of the non-specific reactions that have been reported we now know must have been due to technical errors, though false positives undoubtedly occur. Usually there is no difficulty in differential diagnosis. Kolmer finds the reaction often positive in yaws and in leprosy. Positives have been reported in malaria during the febrile stage, but all of his 11 cases were negative. In scarlet fever the reaction is uniformly negative, though the opinion still prevails that the reverse is true.

Anesthesia and pellagra both are occasionally found associated with positive reactions.

The cerebrospinal fluid is much less subject to error than the blood serum. He has found it positive only in cases of yaws and of leprosy in addition to syphilis.

Baermann and Wetter[8] found no positive reaction in 10 cases of malaria.

Michaelis and Lesser[9] found 1 positive reaction in a large series of malaria cases.

Rudolph Buhman[10] found 5 positives in 99 miscellaneous non-luetic cases; 3 of these cases were tuberculous leprosy, the other 2 were tubercular, and later gave a fairly definite history of lues. Included in the list were 15 cases of scarlet fever and 10 of malaria, in all of whom the reaction was negative.

Craig[11] finds false positives with regularity only in yaws, tuberculous leprosy, some cases of relapsing fever, some malarial infections in the febrile stage only, and in some cases of experimental trypanosomiasis in animals. He says that tuberculosis is more commonly associated with syphilis than any other disease and that syphilis of the lung is not infrequently called tuberculosis. If syphilis

[6] Penna. Med. Jour., 1913, **17**, 217.
[7] Text-book of Infection, Immunity and Specific Therapy, 1915, p. 465 et seq.
[8] Wien. klin. Wchnschr., 1908, **21**, 1765.
[9] Berl. klin. Wchnschr., 1908, **45**, 301.
[10] Tr. Am. Gyn. Soc., 1916, **41**, 319.
[11] Loc. cit.

25-50 per cent; plus-minus, under 25 per cent; and negative, complete hemolysis. In many cases only four instead of five positive degrees are reported.

These five or six reports may, for all practical purposes, be condensed into three—positive, complete inhibition of hemolysis; negative, complete hemolysis; and doubtful, anything between the two. A positive reaction means syphilis if the few other conditions that are still recognized as giving a positive can be excluded. One single negative standing alone is worthless in excluding lues, but is very valuable confirmatory evidence, and a doubtful reaction must be interpreted by the clinician. It is unjust to any patient to diagnose syphilis by the *Wassermann alone,* unless it shows complete or practically complete hemolysis. In a case known to be luetic, a doubtful (one, two or three plus) reaction is an indication for further treatment.[4]

It is the clinician's business to interpret the test; the laboratory should merely report the behavior of the serum when tested. For this reason Craig thinks it better that the laboratory man should not know the history of the case, lest his reading of the test be biassed and erroneous.

There is hardly a disease known in which the Wassermann has not at some time been reported positive, but most often in the other protozoan diseases. So striking used to be the proportion of positives in these cases, that R. Müller, of Vienna,[5] decided that scarlatina could not be a protozoan disease because he so rarely found the Wassermann positive, though he says positives do occur, rarely, in the disease. (I need not say that Müller stands practically alone in this view of the reasons for regarding scarlet fever as non-protozoal in etiology.)

Müller found that in 88 per cent of cases of yaws the Wassermann reaction is positive. He records that the results of different authors in malaria are variable. Bohn, he says, found a positive reaction in 35 per cent of his 46 cases, the reaction disappearing when the malaria was cured.

Bauermann and Wetter (quoted by Müller) using larger material, found only occasionally an incomplete reaction, almost exclusively as the fever was rising. A reaction still positive three days after the disappearance of all fever, in their opinion, signifies lues.

Other non-specific positives are rare. The reasons why they do occur are not known. Müller gives 3 per cent positive in advanced tuberculosis and says that the test is very occasionally positive in various tumors, especially carcinoma, but only when the patient is *in extremis*, with generalized metastases.

Tubercular leprosy shows the large proportion of 19 per cent

[4] See "The Wassermann Test," by C. F. Craig, 1921.
[5] Die Sero-Diagnosé der Syphilis, 1913, Vienna.

of positive reactions, but curiously enough, in Müller's experience, the anesthetic form was invariably negative.

Kolmer and Casselman[6] found the Wassermann to be weakly positive in 19 per cent of cases of psoriasis. Of 250 cases of scarlet fever they found none with a positive reaction.

They record 5 cases of malaria; 3 of these had negative reactions; of the other 2, 1 was frankly luetic. The history of the other patient was not obtained. In discussing this paper, Dr. John A. Roddy, of Philadelphia, said that in the Canal Zone, during the summer of 1913, he saw hundreds of cases of malaria on whose serum a Wassermann reaction was performed, with uniformly negative results.

Kolmer[7] says the reaction is highly specific, but is so beset with technical difficulties that much confusion has been caused. Many of the non-specific reactions that have been reported we now know must have been due to technical errors, though false positives undoubtedly occur. Usually there is no difficulty in differential diagnosis. Kolmer finds the reaction often positive in yaws and in leprosy. Positives have been reported in malaria during the febrile stage, but all of his 11 cases were negative. In scarlet fever the reaction is uniformly negative, though the opinion still prevails that the reverse is true.

Anesthesia and pellagra both are occasionally found associated with positive reactions.

The cerebrospinal fluid is much less subject to error than the blood serum. He has found it positive only in cases of yaws and of leprosy in addition to syphilis.

Baermann and Wetter[8] found no positive reaction in 10 cases of malaria.

Michaelis and Lesser[9] found 1 positive reaction in a large series of malaria cases.

Rudolph Buhman[10] found 5 positives in 99 miscellaneous non-luetic cases; 3 of these cases were tuberculous leprosy, the other 2 were tubercular, and later gave a fairly definite history of lues. Included in the list were 15 cases of scarlet fever and 10 of malaria, in all of whom the reaction was negative.

Craig[11] finds false positives with regularity only in yaws, tuberculous leprosy, some cases of relapsing fever, some malarial infections in the febrile stage only, and in some cases of experimental trypanosomiasis in animals. He says that tuberculosis is more commonly associated with syphilis than any other disease and that syphilis of the lung is not infrequently called tuberculosis. If syphilis

[6] Penna. Med. Jour., 1913, **17**, 217.
[7] Text-book of Infection, Immunity and Specific Therapy, 1915, p. 465 et seq.
[8] Wien. klin. Wchnschr., 1908, **21**, 1765.
[9] Berl. klin. Wchnschr., 1908, **45**, 301.
[10] Tr. Am. Gyn. Soc., 1916, **41**, 319.
[11] Loc. cit.

be excluded, tuberculosis does not give a positive reaction. If the positive Wassermann in malaria persists after the disappearance of all fever, syphilis is a complication in the opinion of Craig and other observers.

Anesthetic leprosy is never positive; even in the nodular form it is difficult to be dogmatic, for this disease occurs almost exclusively among savage or uncivilized races, which are so thoroughly permeated with syphilis that to exclude it is very difficult in any given case.

A large percentage of positives in non-luetic conditions, in Craig's opinion, means faulty technic in the laboratory.

In 2643 non-luetic cases on whom the test was performed by this observer,[12] only 11 positives were found, 0.4 per cent. Four of these cases had malaria and the reaction disappeared with the fever. The other cases were divided as follows: tuberculosis 3; pityriasis rosea, 3; diagnosis not made, 1. Two of the tuberculous patients later gave suspicious histories and cleared up under antispecific treatment.

M. O. Biggs,[13] reports 10 cases of "thyroidogenous psychosis," with varied mental symptoms and the ordinary symptoms of Graves's disease. In no case was there any evidence of lues either on physical examination or in the personal or family history. In every case the blood Wassermann was more or less strongly positive. None of these patients were operated upon nor was spinal fluid Wassermann done.

He reports 1 more case, not insane, a woman with Graves's disease of rather severe degree, of twenty-five years' standing. Her history and physical examination were entirely negative; Wassermann was positive at the time of operation. The operation was entirely successful. One year later the patient was symptom-free and her Wassermann was negative. No antiluetic treatment had been taken.

Jean Golay[14] gives the results of his experience in the following table:

Diagnosis.	No. of Specimens.	Negative.	Positive.
Health	13	13	
Scarlatina	19	18	1 weakly positive
Tuberculosis	13	12	1 weakly positive
Neoplasms	9	9	
Diabetes	1	1	
Pneumonia	2	2	
Icterus	3	1	2 weakly positive

A. Touraine[15] says that the reaction is usually positive in spirochetal and trypanosomal diseases. In chronic malaria he finds

[12] Craig, C. F.: Am. Jour. Med. Sc., 1915, **149**, 41.
[13] Jour. Missouri Medical Association, 1919, **16**, 326.
[14] Internat. Clinics, 1920, **4**, 79.
[15] Rev. de Méd., 1920, **37**, 103.

it always negative. In the acute form he very often finds it positive during the rise of the fever (202 cases out of 326) subsequently becoming negative.

He considers the reaction to be not infrequently positive in acute fevers in general, disappearing with the fever. In chronic infections —tuberculosis and leprosy—it is much less frequent. He says the reaction is often positive after anesthesia with ether and especially with chloroform, but never after nitrous oxide.

In the Hospital of the University of Pennsylvania, between 1906 (when the Wassermann reaction was first reported) and February, 1921, 75 cases of malaria occurred, but not until 1916 was a Wassermann done routinely on all cases. The earlier tests were done only where the history was suspicious or the diagnosis for a time in doubt. Twenty-one tests in all were done on malaria patients, but only 8 of these were routine.

Of these 21 cases the Wassermann was negative in 12, of which 3 were routine. In 6 cases the reaction was positive, in the presence of either a frank venereal history, or one strongly suspicious, *e. g.*, admission of gonorrhea, multiple miscarriages in wife, generalized adenopathy, etc. One case had a doubtful reaction with negative history; 1 other with suspicious history had anticomplementary serum and the test was not interpreted. This patient, however, was considered luetic at the time and a later Wassermann was positive outside. In only 1 case of the 21 tested was there a completely negative luetic history, with a weakly positive reaction. Concerning this patient, a young colored girl, Dr. George V. Janvier, of Lansdowne, Pa., her physician, reports that he has not seen her since she entered the hospital, and he knows nothing of her subsequent history.

In no case was the reaction repeated in the hospital, even in the probably syphilitic cases, nor is there any record of the time in the malarial cycle when blood was drawn for the test. It would be very interesting and important to know this in the 2 cases with positive reactions and negative histories, but there is at present no way of finding this out.

In the Philadelphia General Hospital since 1910 there have been a total of 154 cases of malaria. Here, also, the Wassermann was not done as a routine measure but only in suspicious cases. In fact, 130 of the 154 cases were *not* tested. Of the remaining 24 the reaction was negative in 15, and 9 cases were either frankly luetic or lues could not be excluded. Here, also, the reaction was not repeated in the hospital and no record was made of the time in the malarial cycle when blood was drawn.

In the Pennsylvania Hospital from 1910 to the end of 1920 there have been 232 cases of malaria, of which only 27 were subjected to the Wassermann reaction. Of these 20 were negative, 6 were positive, but lues was not excluded. One case showed a false

positive. This is the only case I have seen in which the time of drawing blood could be established and where the reaction was repeated with negative results.

CASE—J. F., admitted to the Pennsylvania Hospital August 30, 1914, suffering with malaria: Venereal history negative—denied venereal and the physical examination was likewise negative. He had a chill August 30, the day of admission, and one the next day, but none thereafter. On September 1 his Wassermann was reported positive on blood that was therefore taken either during or very shortly after a chill. He was discharged very much improved on September 4, and his second Wassermann was reported negative on September 5, the next day. It seems likely that blood for this test was taken on September 4—or at any rate long enough after his last chill for the malaria to have ceased to influence his serum.

To summarize, 461 cases of malaria have been examined; 73 of these, or 16 per cent, were subjected to the Wassermann test. Of these 73, 23, or 32 per cent, were positive, with lues not satisfactorily excluded; 47, or 65 per cent, were negative, and 3, or 4 per cent, showed a positive reaction, when lues could definitely be ruled out, as far as history and physical examination will allow.

These figures are inconclusive, though as far as they go they are in accordance with those given by various authors quoted above, with the exception of Touraine, who found the elevated proportion of 202 positives out of 326 malaria patients tested. I cannot explain his results other than by assuming that he was not careful to exclude lues or that his laboratory was at fault. However, to speak definitely, we should have to know what the reaction was in those 389 cases I report who were not tested.

Tuberculosis. The last 500 cases of tuberculosis occurring in the Philadelphia General Hospital were studied. The great majority of these were severe and far advanced cases, for the incipient cases rarely come to this hospital. Here, also, the great majority of the cases were not tested—only 179 tests or a little over 35 per cent; the reaction was more often done here when the physical examination and history were negative than in the malaria cases.

Of the 179 cases in which the reaction was tested, 38, or 20 per cent, were either frankly luetic or lues was not excluded to my satisfaction; 135, or 76 per cent, were negative, and 6, or 45 per cent, had a reaction more or less strongly positive, in the presence of a negative history and physical examination. I append abstract histories of these 6 cases:

1. W. E., severely ill with pulmonary tuberculosis. History and physical examination negative for lues. Sputum positive for tuberculosis.

Wassermann: Cholesterinized antigen, double plus; Noguchi antigen, plus; luetic antigen, plus.
No antiluetic treatment; later all antigens negative.
Patient died of tuberculosis June 23, 1920. No autopsy.

2. J. C., admitted with advanced pulmonary tuberculosis. History and physical examination negative for lues. Sputum positive for tuberculosis.
Wassermann: Cholesterinized antigen, plus; Noguchi antigen, negative; luetic antigen, negative.
Not repeated.
Died August 9, 1920. No autopsy.

3. F. P., admitted with advanced pulmonary tuberculosis. History and physical examination negative for lues. Sputum positive for tuberculosis.
Wassermann: Cholesterinized antigen, plus; Noguchi antigen, negative; luetic antigen, negative.
Subsequently repeated with same result.
Died August 29, 1920. No autopsy.

4. A. S., admitted with advanced tuberculosis. History and physical examination negative for lues. Sputum positive for tuberculosis.
Wassermann: Cholesterinized antigen, plus; Noguchi antigen, negative; luetic antigen, negative.
Not repeated.
Died September 18, 1920. No autopsy.

5. Anna S., admitted with advanced pulmonary tuberculosis. History and physical examination negative for lues. Sputum positive for tuberculosis.
Wassermann: Cholesterinized antigen, double plus; Noguchi antigen, negative; luetic antigen, negative.
Not repeated.
Died September 17, 1920. No autopsy.

6. C. H., admitted with acute tuberculous pneumonia, gravely ill. History and physical examination negative for lues. Sputum filled with tubercle bacilli.
Wassermann: Cholesterinized antigen, double plus; Noguchi antigen, negative; luetic antigen, negative.
Not repeated.
Died December 18, 1920. Autopsy confirmed antemortem diagnosis, and showed many other tuberculous lesions as well, but no evidence of lues, either grossly or on microscopic examination.

It will be noted that in all these cases three antigens were employed. In 5 of these cases the cholesterinized antigen alone was positive; only once did the other antigens react positively also. Of course it is impossible to speak dogmatically from only 6 cases, but this seems to show a hypersensitiveness on the part of this antigen that would detract somewhat from its value in diagnosis. It was indeed remarkable in looking over the hospital records to see how often the cholesterinized antigen would be strongly positive while the other two were either weakly positive or negative.

Hyperthyroidism. A study of the cases of hyperthyroidism and exophthalmic goiter cases in the Philadelphia General Hospital and University Hospital was made, but it was found that the Wassermann was so seldom done on these cases in the Philadelphia Hospital and in the surgical wards of the University that nothing was revealed. The same was true of the medical wards of the University before 1915.

After 1915 there were a total of 90 cases of Graves's disease and hyperthyroidism in the medical wards of the University. Of these, 1 (1.1 per cent) had frank lues and 38 (42.2 per cent) were not tested. The remaining 51 (56.6 per cent) cases had negative Wassermanns. A total of 13 tests were also done in the surgical wards and at the Philadelphia General Hospital, and these 13 were also negative. In only 1 case of 103 examined was a positive Wassermann found, and that patient had definite lues.

This is contrary to the statement of Biggs above, but I believe is in line with the experience of others.

Drs. D. J. McCarthy, C. H. Frazier and George W. Norris, all of Philadelphia, inform me that in their very extensive experiences with hyperthyroidism they have not met with any cases associated with a positive Wassermann.

It is proverbially impossible to prove a negative, but in Philadelphia at least the proportion of positive Wassermanns in hyperthyroid cases seems to be much less than in the general run of unselected hospital admissions. The small number of cases I present shows no evidence that hyperthyroidism stands in any causal relation to the Wassermann reaction.

	Wassermann positive and lues excluded.	Wassermann negative.	Wassermann positive and lues not excluded.	Wassermann not done.
Malaria.				
	3	47	23	388
Tuberculosis.				
	6	135	38	321
Exophthalmic Goiter.				
	0	64	1	108
Totals	9	246	62	817

Conclusions. 1. The Wassermann reaction is invariably positive at some time during the course of syphilis, if properly performed, and at sufficiently frequent intervals.

2. It is but rarely positive in non-luetic diseases.

3. It is unusual for it to be positive in malaria. If positive, it is only weakly so (doubtful in Craig's classification) while the fever is rising, becoming negative between paroxysms.

4. It is rarely positive in tuberculosis, and when positive the reaction is weak or doubtful (*i. e.*, not diagnostic of lues in the absence of history or signs). I have found it positive only in far-advanced cases shortly before death.

5. It is not positive in uncomplicated hyperthyroidism.

6. The cholesterinized antigen is probably too delicate to be of value alone in diagnosing lues when there is no history or physical evidence of disease. It is invaluable in following the course of known syphilis under treatment, by reason of its delicacy.

I desire to express here my deep gratitude to Dr. Edward B. Krumbhaar, director of laboratories, Philadelphia General Hospital, for his unfailing kindness and great courtesy to a beginner in medicine.

A FURTHER NOTE UPON A COMPARISON OF THE SACHS-GEORGI AND WASSERMANN REACTIONS IN THE SEROLOGIC DIAGNOSIS OF SYPHILIS.

By Robert A. Kilduffe, M.D.,

DIRECTOR OF LABORATORIES, PITTSBURGH HOSPITAL; DIRECTOR OF LABORATORIES, MCKEESPORT HOSPITAL; SEROLOGIST, PROVIDENCE HOSPITAL.

(From the Laboratories of the Pittsburgh Hospital.)

In a former communication[1] a report was made of the results obtained with the Sachs-Georgi reaction in a series of 296 serums simultaneously subjected to the Wassermann test.

At that time, as the result of the observations made and recorded, the conclusion was reached that "A diagnosis of syphilis or conclusions as to treatment cannot be based upon the results of a Sachs-Georgi test with safety and the reaction is not suitable for general use for this purpose."

Since the publication of this report several others appeared both in foreign and American literature. The foreign reports were almost uniformly favorable, while those of American literature, though varying to some extent, were, in the main, corroborative

[1] Kilduffe, R. A.: A Comparison of the Wassermann and Sachs-Georgi Reaction in the Serologic Diagnosis of Syphilis, Arch. Dermat. and Syph., April, 1921, **3, 1,** 415.

of the usefulness of the test. Notable among these are the papers of Hull and Faught[2] and Levinson and Peterson.[3]

The former observers, using a modification of the test in which the test serum is used undiluted in amounts of 0.3 cc, found that their modified reaction agreed with the Wassermann in 88 per cent of 296 serums tested by both methods.

Levinson and Peterson, reporting upon 1042 comparative tests using the modification proposed by Mandelbaum,[4] in which the serum is diluted in the proportion of 3 drops to 1 cc of normal saline solution, with the incubation period in the hot-air incubator lengthened to eighteen to twenty-four hours, followed by twenty-four hours at room temperature, found that the two reactions agreed in 92 per cent of the cases tested.

Immediately following the conclusion of the first series published from these laboratories, and in view of the varying results recorded elsewhere, it was thought that perhaps the antigen used had not sufficient delicacy, and a new antigen was thereupon prepared and a new series inaugurated, the results of which are herewith reported.

In the preparation of the antigen the technic as given by Galli-Valerio[5] was adhered to, as it seems to be that used by all investigators publishing their technic. Absolute alcohol was used throughout and Merck's cholesterin for the cholesterinization of the alcoholic extract. Before cholesterinization the alcoholic beef heart was titrated and found to be anticomplementary in 2.5 cc of 1 to 20 dilution and antigenic in 0.04 cc of 1 to 20 dilution. After the addition of the further 200 cc of alcohol and the 1 per cent alcoholic cholesterin solution (13.5 cc) the anticomplementary titration remained the same while the antigenic unit had fallen to 0.1 cc of 1 to 20 dilution, probably because of the further dilution of the extract by the added alcohol. This antigen was then added to a series of known positive and negative serums in order to determine that precipitation would occur in a sufficient number to indicate its availability for use in the test.

A series of 430 serums was then subjected to parallel Wassermann and Sachs-Georgi tests by the following technic:

Technic of the Tests. Sachs-Georgi: The antigen prepared and titrated as indicated above was diluted 1 to 5 with sterile salt solution (0.85 per cent), one part of the saline being added slowly with gentle shaking and the remaining four parts added more rapidly, the shaking being continued. The resultant solution was turbid and milky.

[2] The Sachs-Georgi Precipitation Test for Syphilis, Jour. Immunol., November, 1920, **6**, 521.

[3] The Sachs-Georgi Reaction for Syphilis, Arch. Dermat. and Syph., March, 1921, **3**, 286.

[4] München. med. Wchnschr., 1918, **65**, 204, quoted by Levinson and Peterson.

[5] Corr.-Bl. f. schweiz. Aerzte, December 25, 1919, **49**, 1978.

Serums: The serums used in the series comprised those taken for diagnosis in the wards of the Pittsburgh Hospital; serums taken as a routine in the gynecologic and obstetric services of the hospital, and those of cases handled through the Morals Court, these last being obtained through the coöperation of Dr. A. H. Eggers, County Medical Inspector, Pennsylvania State Department of Health. In this latter group were known syphilitics, suspects and cases under treatment. A sufficient number of normal Wassermann-negative serums were included in the series to serve as an adequate control.

No serum used was over forty-eight hours old, and many were tested within twenty-four hours of their receipt. All were clear, free from blood and inactivated for fifteen minutes at 56° C.

For the test 0.1 cc of serum was placed in a serologic test-tube and 0.9 cc of sterile 0.85 per cent salt solution added, thus giving 1 cc of a 1 to 10 dilution, to which 0.5 cc of the Sachs-Georgi antigen was added and the tubes gently shaken. They were then placed in the hot-air incubator for eighteen to twenty-four hours, a preliminary reading made and then allowed to stand at room temperature for twenty-four hours, after which the final reading was made. A known negative and positive were always included. Readings were made by transmitted light, using a modified agglutinoscope and recorded as follows:

++++ Well-marked precipitate plainly discernible.
+++ Perceptible precipitate not so marked as ++++.
++ Perceptible precipitate not so heavy as +++.
+ Barely discernible trace of precipitate.
− No precipitate.

Technic of the Wassermann Test. All serums were submitted to the Wassermann test at the same time by the following technic:

Sheep Cells: Sheep bled the day preceding the test, cells washed until free from serum (four to six washings in normal saline) and used in dose of 0.5 cc of a 2.5 per cent suspension.

Amboceptor: Glycerinated serum diluted with normal saline according to titer and used in dose of 0.2 cc.

Complement: The pooled serum of two to four guinea pigs diluted 1 to 10 with 0.85 per cent salt solution. Each day preceding the main test, complement was titrated against 0.5 cc of 2.5 per cent sheep-cell suspension in the presence of 0.1 cc of amboceptor and the unit read as the smallest amount producing complete hemolysis in one hour in the 38° C. water-bath. Two units were used in the test.

Antigens: A triple battery was used for each serum, consisting of cholesterinized (0.4 per cent) extract of human heart; acetone-insoluble lipoids of human heart; and an alcoholic extract of syphilitic fetal liver. The dose was determined by antigenic and anticomplementary titrations, the amount used being always from two to five times the antigenic unit, which amount was always from five to ten times less than the anticomplementary unit.

The Test: Each serum was used in dose of 0.2 cc and the complement in dose of two titrated units of 1 to 10 dilution. Incubation was in an iced water-bath at a temperature of 2° to 4° C. for one hour. At the end of the preliminary incubation the tubes were placed in the 38° C. bath for five minutes and then the cells and amboceptor added and the test reincubated in the 38° C. bath until all controls were hemolyzed.

Antigen, corpuscle, amboceptor, complement and positive and negative controls were always added. The same antigens were used throughout the tests.

Results were recorded according to the degree of fixation obtained with each antigen separately and the strength of the reaction graded accordingly. A serum was looked upon as positive if 50 per cent or over of inhibition of hemolysis occurred with the cholesterin antigen alone, even though the other two antigens were negative as, on the the basis of data elsewhere recorded,[6] and as said by Kolmer,[7] "I have learned from experience to place reliance upon results obtained with a properly prepared and titrated cholesterinized extract."

Results of Comparison of the two Reactions. A total of 430 cases was subjected to parallel tests as above outlined. Of these 102, or approximately 23 per cent, gave plus- four fixations, the high percentage of positive cases being largely due to the inclusion in the series of the Morals Court serums, in which a high percentage of positive findings was to be expected, which, for the purpose of this investigation, was to be desired.

Of the Wassermann positive cases, as shown in Table I, the Sachs-Georgi was positive in 30 and negative in 72.

TABLE I.—RESULTS WITH WASSERMANN POSITIVE SERUMS.*

Number of serums.	Sachs-Georgi reaction.					Sachs-Georgi positive.	Sachs-Georgi negative.
	++++	+++	++	+	−		
102	11	5	10	4	72	30	72

* Includes serums positive with cholesterinized antigens only.

Table II shows the results obtained with 324 Wassermann negative serums in which the Sachs-Georgi reaction gave 32, or approximately 10 per cent of positive results.

[6] Kilduffe, R. A.: Concerning the Specificity of Cholesterinized Antigens in the Serologic Diagnosis of Syphilis, Arch. Dermat. and Syph., May, 1921, **3**, 598.

[7] The Serum Diagnosis of Syphilis and Gonorrhea Employing Human Complement, Am. Jour. Syph., October, 1918, **2**, 739.

TABLE II.—RESULTS WITH WASSERMANN NEGATIVE SERUMS.

Number of serums.	Sachs-Georgi reaction.					Sachs-Georgi positive.	Sachs-Georgi negative.
	++++	+++	++	+	–		
324	6	18	3	5	292	32	292

Four anticomplementary serums were all positive to the Sachs-Georgi test.

TABLE III.—RESULTS WITH ANTICOMPLEMENTARY SERUMS.

Number of serums.	Sachs-Georgi reaction.					Sachs-Georgi positive.	Sachs-Georgi negative.
	++++	+++	++	+	–		
4	2	1	1	0	0	4	0

In the first series similar results were obtained and, for the purpose of consolidation, the combined results of both series are shown in tabular form.

TABLE IV.—COMBINED RESULTS WITH WASSERMANN POSITIVE SERUMS.*

Number of serums.	Sachs-Georgi reaction.					Sachs-Georgi positive.	Sachs-Georgi negative.
	++++	+++	++	+	–		
162	15	5	13	14	115	47	115

* All positive serums, including cholesterin plus only in both series.

TABLE V.—COMBINED RESULTS WITH WASSERMANN NEGATIVE SERUMS.*

Number of serums.	Sachs-Georgi reaction.					Sachs-Georgi positive.	Sachs-Georgi negative.
	++++	+++	++	+	–		
544	11	18	7	18	490	54	490

* Includes serums of both series.

TABLE VI.—COMBINED RESULTS WITH ANTICOMPLEMENTARY SERUMS.*

Number of serums.	Sachs-Georgi reactions.					Sachs-Georgi positive.	Sachs-Georgi negative.
	++++	+++	++	+	−		
20	2	1	1	2	14	6	14

* Includes serums of both series.

A study of the tables shows that of 162 Wassermann positive serums, 47, or approximately 29 per cent, were positive to the Sachs-Georgi reaction as here performed, and that in 544 negative serums the Sachs-Georgi reaction was also positive in approximately 10 per cent.

Of 20 anticomplementary serums, 6, or approximately 30 per cent, gave positive Sachs-Georgi reactions.

Every effort was made throughout the present series to make the tests strictly parallel and to perform the Sachs-Georgi reactions with great care in view of the variance from the results obtained by other investigators. The results are obvious and indicate either that the conclusions previously drawn may be reaffirmed and looked upon as corroborated or that the Sachs-Georgi reaction was improperly performed. The only deviation from the original technic was the substitution of 1 cc of 1 to 10 dilution for 10 cc of the same dilution (1:10), and it is not felt that this had any appreciable influence upon the results obtained.

Summary. The results of 430 parallel Wassermann and Sachs-Georgi reactions are reported and coördinated with a series of 296 previously reported.

Conclusions. The following conclusions, previously stated, are reaffirmed upon the basis of the results herewith reported:

1. The Sachs-Georgi test is often difficult to read.
2. The reaction is neither as delicate nor as trustworthy as the Wassermann test.
3. The Sachs-Georgi reaction may be positive with Wassermann negative serums and negative with Wassermann positive serums in relatively high percentage of cases.
4. The number of non-specific reactions is sufficiently high to render the test unreliable as a means of diagnosis.
5. A diagnosis of syphilis, or conclusions as to the results of treatment, cannot be based upon the results of a Sachs-Georgi reaction with safety, and the reaction does not seem suitable for general use for this purpose.

TREATMENT OF SYPHILIS AMONG THE INSANE.

By Thomas B. Christian, M.D.

PATHOLOGIST TO THE STATE HOSPITAL AT MORRIS PLAINS, NEW JERSEY.

At the present time among the hospitals for the insane we are receiving our share of syphilitics. According to the cases in this hospital at least 95 per cent belong in the tertiary class or latent types. In a number of state hospitals all the syphilitics are put under antisyphilitic treatment while in a great majority of them they are not treated. The reason for their not being treated is probably due to the fact that many syphilologists contend that latent syphilis cannot or never can be cured, that is in so far as producing a permanent negative Wassermann is concerned. But is this excuse a justifiable one for not using the methods we have for trying to hold in check this disease? It has been and is now the plan of the U. S. P. H. Service and state boards of health to eradicate syphilis, and to encourage this a number of states have enacted laws declaring syphilis a reportable disease and have established free clinics for treatment of the same.

In insane hospitals we have three distinct types of syphilis to deal with: (1) Cases showing a four-plus Wassermann and a negative spinal fluid with no clinical manifestations of syphilis, this constituting the majority class; (2) cases with a positive Wassermann reaction—a negative spinal fluid—but clinical manifestations of syphilis present, and (3) psychosis with syphilis as the etiologic factor—as general paralysis, taboparesis and tabes with psychosis.

At the present time we are treating all cases of syphilis with a four-plus Wassermann with or without clinical manifestations, including a few selected cases of general paralysis.

It has been, and still is, argued by some eminent syphilologists that patients with a positive Wassermann and with no lesions should not be treated. The basis for their belief is that once infected with syphilis a patient carries it with him to his grave. However, I doubt if anyone has followed a single case of syphilitic infection from the initial lesion to his last day to prove the statement of once syphilitic always syphilitic. Ninety-five per cent of our cases of syphilis belong in the tertiary or latent class with no active lesions and no other signs except a positive Wassermann and the mental symptoms of the paretics. Many of them give a history of a previous chancre—some with treatment while others have had no treatment previous to coming to this institution. We also get a number of positive Wassermanns and paretics that had negative histories of initial chancres.

The chances of obtaining a negative Wassermann in cases of latent syphilis, even in very old cases, have been shown to be good,

and therefore such patient should be treated regardless of the mental condition, although a negative Wassermann obtained after a few months of treatment does not indicate that a cure has been effected. Syphilis in itself is an entity and must be treated as such. Whether syphilis is associated with a disease either functional or organic it should be treated. It must be treated as syphilis regardless of whether the mental condition is caused by it or not, and it must be treated vigorously.

Many of the cases admitted here are recognized too late for curative treatment, but there is no reason to let it stand and not try to check the onward progress of the disease. In treating such cases I have found many improvements among the patients even though no complete cure was obtained nor expected. These cases of incurable syphilis would probably never have reached us if they had been treated over long periods of time at the beginning of their infection and until the serum Wassermann and spinal fluid Wassermann were negative.

We do not treat cases of general paralysis expecting a cure, but only to ameliorate their symptoms and hold in check the progress of the fatal disease. In such cases we cannot agree with other men who have worked along this line and found cures and improvements. Some time past we treated vigorously a series of paretics, watching the effect upon the mental condition and blood and spinal fluid, but our conclusions resulted in 2 out of 20 slightly mentally improved and 3 showed a paretic gold curve changed to that of a luetic zone curve.

The two slightly improved cases showed a drop of the Wassermanns to two-plus, but the spinal fluid remained four-plus. About 15 cases showed no change in Wassermanns nor clinical improvement. I have had physicians tell me that it has been their experience to see cases of well-pronounced paresis which had remissions of the disease lasting from one to four years, which followed intraspinal injections. I have also seen similar cases which had remissions of the disease which had no antisyphilitic treatments. We have also received far-advanced cases of paresis that were treated in other institutions and left improved or cured according to their records when in reality they were in a normal remission that occurs in a number of cases of paresis.

It is not, in my opinion, an invasion of the brain from five to twenty years after the primary sore which suddenly appears with speech disturbances and grandiose ideas to the patient's death from two to three years. The spirochetes are deposited in the cerebral cortex during the period of generalization of the organisms, as in aortitis and visceral syphilis, where they may remain without reactive phenomena or the spirochetes hidden away in the deeper parts of the brain may act in the same way as in other organs. The spirochetes were probably there from the beginning

and a spinal puncture at that time would have shown the condition present with no clinical signs. We have no case here on record which shows a positive blood and negative spinal fluid and showing a number of years later a positive spinal fluid. If the general practitioner wishes to save his patients infected with syphilis from the dreaded disease of paresis he should obtain a spinal-fluid examination upon every case of syphilis he treats.

Fordyce[1] states that neurosyphilis appears first by pathologic findings in the spinal fluid before clinical symptoms appear. That the tissues may harbor the treponema for an indefinite time with little or no evidence of their presence and that the nervous system may be the habitat of the organisms with little or no tissue reaction until a traumatism or some exciting factor stimulates their activity or until sufficient time elapses to permit centers or tracts to be compromised, which then give rise to objective signs and symptoms. Judging from the above every case of paresis we have in this institution would have shown serologic signs of nervous tissue involvement if a spinal examination had been performed at the time of the general dissemination of the spirochetes. It has been and is now the idea of many that it takes ten to twenty years for paresis to develop after the initial infection, which is true if based upon the clinical syndrome of physical and mental symptoms but not true if based upon the serologic findings in the spinal fluid. Substantiating this statement Fordyce[1] quotes a very interesting case as follows: Patient had chancre on October 20, 1919, and on April 9, 1920, the examination of the blood serum was four-plus; spinal fluid showed 22 cells; four-plus globulin, four-plus Wassermann to 0.1 cc and a gold curve of 5555432100, which is a typical serologic syndrome of paresis. None of the mental and physical signs of paresis were present. Judging from the above case the cases of general paralysis we admit here must have had the laboratory picture of paresis from ten to twenty years before admission and a sufficient length of time must pass to produce the clinical picture of paresis. Therefore it would seem highly improbable that after such a length of time the spirochetes have inhabited the body and produced destructive pathology in the brain that intraspinal therapy is not indicated in institutionalized cases. We have discontinued the intraspinal therapy among the paretics, as our cases are too far advanced for treatment, and our previous treatment in this type of cases gave us no encouraging results. The degenerated nervous tissue is entirely too sensitive for taking care of the irritating salvarsanized serum, as we have had several serious reactions following such treatments. Intraspinal therapy is, however, indicated in early selected cases of neurosyphilis as syphilitic meningitis, meningoencephalis or meningomyelitis, and is a safe procedure if proper technic is used.

[1] Am. Jour. Med. Sc., No. 3, **156**, 313.

We treat a few selected cases of paresis with the idea of holding in check the disease by prolonged treatments of salvarsan and mercury. Previous to administering the salvarsan we drain the spinal canal. This is supposed to enable more arsenic to be transmitted to the nervous tissue from the blood by the vascular meninges and choroid plexus. This method is used by a number of syphilologists with the above idea while others claim it has no effect. I have for some time past drained the spinal canal in excited cases and cases in convulsions, and by thus relieving the pressure they have been relieved. Many paretics in the last stages, however, show a decreased pressure of the spinal fluid.

Every patient admitted to this hospital has a blood Wassermann performed and all cases showing positive bloods is subjected a spinal puncture, and in addition spinal punctures are performed in those cases with a negative Wassermann giving a previous history of a positive Wassermann of initial chancre, those with clinical signs of syphilis and those showing suspicious neurologic signs. We have found a number of cases with positive spinal fluids with a persistent negative blood Wassermann. A number of cases of neurosyphilis are detected only by resorting to spinal puncture. Making serologic examinations upon many of the old cases that have been here from ten to twenty years we have discovered a number of interesting cases. The following example will give examples of other cases:

F. S., admitted in 1908, gave a negative family history, negative venereal history and no signs of syphilis. No Wassermann, however, was performed. His mental picture was that of a dementia precox. During the past year his symptoms have been taking on that of a paresis. On October 12, 1921, for the first time a blood and spinal examination was performed and gave a typical serologic syndrome of paresis. His diagnosis was changed to general paralysis. Was this a case of syphilitic psychosis from the beginning or a case of dementia precox with neurosyphilis, later being a mixed case of paresis superimposed upon dementia precox or a case of early paresis from the date of his admission? Is paresis and taboparesis the only form of insanity which we have as a direct cause of syphilis? Why cannot the spirochetes infect other portions of the brain and give a clinical picture entirely different from paresis and simulating other forms of insanity, the causes of which are unknown? This question has been discussed by eminent psychiatrists, and is one we wish to determine in the future.

If more examinations of the spinal fluid were made in general hospitals and private practice I am convinced that many cases would probably never reach institutions for the insane. The activity of a syphilitic process in the central nervous system is indicated earlier, more accurately and a number of times only by

pathologic changes in the spinal fluid, and the activity of syphilis of the nervous system is shown by the globulin test, cell count, Wassermann and gold solution reaction long before mental symptoms or physical signs are present. Failure to recognize the importance of spinal-fluid examinations leads us to overlook many cases of slow-progressing cases of neurosyphilis until the physical signs and mental symptoms are present, and then it is too late for treatment with the expectation of a cure. I see no reason why anyone should wait until advanced degeneration in important organs is present and stand helpless in its presence when by the simple procedure of a spinal puncture this may be averted. And a great number of times it is the physician's fault, as no case should be discharged as cured without a negative spinal fluid as well as a negative blood. I realize the fact that many patients will not submit to a spinal puncture, and I have met with the same hindrances, but after explaining the importance of the procedure the simplicity of the process and no after dangers they will realize they will have nothing to loose and all to gain.

No case of syphilis should be considered cured after a certain number of doses of salvarsan and mercury. Every individual should be treated different, as some cases will obtain a rapid cure, both clinically and serologically, while others must have treatment over a long period of time.

Syphilis is very insidious in its attack on the brain and central nervous system, and our only protection is a continuous follow-up in the after-treatment of its victims. I have seen a number of cases that fall into the hands of so-called syphilologists and have been discharged as cured and terminated in institutions for the insane as a direct result of syphilis. The following case illustrates a number of others:

Mr. M. F., at the age of twenty-five years, contracted syphilis, and during the primary stage was given six intravenous injections of salvarsan followed by twelve of mercury. He cleared up clinically and a Wassermann obtained one month, three months and four months after treatment had been discontinued was negative, but no spinal-fluid examination was performed. He was admitted here a few weeks ago at the age of thirty-seven years, with a clear mental, physical and laboratory picture of general paralysis.

Of course, one cannot say to a certainty that this or other cases here in similar condition would have been cured had the proper treatment been given them years previous to the outbreak of the mental symptoms and physical signs. But we do know that these cases were not treated over prolonged periods and no spinal-fluid examination was performed to determine if intraspinal therapy was indicated, but were pronounced cured after a definite course of treatment, some without a Wassermann, others with one negative

Wassermann, and others with a number of negative Wassermanns, but none with a spinal-fluid examination. And as far as the condition of the patient is concerned a serologic cure is far more important. It is a waste of time to treat cases of general paralysis after mental symptoms and physical signs have set in, as we have seen a number of cases treated vigorously by intravenous-spinous and intraventricular, but no results were obtained.

In general the following is the outline of the method of treatment we use in treating syphilis without spinal involvement: Each patient received ten to twelve injections of salvarsan, the dose depending upon the weight and physical condition of the patient. These injections are given weekly with an intramuscular injection of mercury coming midway between the salvarsan treatments. During the treatment a weekly examination of the urine is performed, and if evidence of nephritis is found, blood chemistry and functional tests were performed, and if the function is shown to be impaired, treatment is discontinued until cleared up. Also a weekly Wassermann and Hecht-Gradwohl test is performed to determine the effect of treatment, the Wassermann being quantitative, the results of which I expect to give more in detail in a later paper. At the end of ten to twelve weeks, which gives the patient from ten to twelve injections of salvarsan and mercury, we take the Wassermann, and if found negative wait until the lapse of one month; take another blood test, if negative then do a third after the third month; and if still negative, we perform a spinal puncture; and if this is negative we pronounce the case as temporarily cured. Now after the elapse of one year another blood test is performed, and if still negative the case is serologically cured. If at any time the blood or spinal fluid is found positive, continue treatment. Those with spinal fluids positive should be given intraspinal therapy. This same plan is followed in private cases as well as institutionalized cases.

If necessary a case can be treated from two to three years with mercury, and salvarsan if administered at long periods and carefully watching the kidneys, liver and skin symptoms. Cases requiring a large amount of salvarsan and mercury should be given a diet consisting mostly of eggs and milk, with an occasional hot-pack for elimination. I do not think there is any advantage in the intensive treatment plan in latent and tertiary syphilis. As to cases showing chancres and secondary lesions I agree with Thom[2] when he states, "Unless treated intensively I desire to go on record as saying that syphilis is, in the vast majority of cases, an incurable disease in so far as rendering a positive Wassermann negative, which after all is the only criterion of cure we have."

[2] Am. Med., May, 1921, new series, No. 5, **16**, 230–340.

From our last 700 injections of salvarsan we have had only two severe reactions, both cases recovering. One was a severe exfoliative dermatitis following the tenth weekly injection and the other a severe jaundice following the third injection. Both cases were taken off salvarsan and given mercury, with good results. The case with the exfoliative dermatitis was a paretic, and three weeks after his last injection his blood test was brought from four-plus to negative, although his spinal fluid remained unchanged as well as his mental condition.

How long should antisyphilitic treatment be continued in latent syphilis? It should be continued until the blood and spinal fluid become negative and continue to be negative at least six months after treatment has been discontinued. If toxic symptoms appear during treatment and a distinct nephritis shown by examination of the urine a sufficient rest will clear them up and treatment can be continued. It has been shown by Anderson[3] that although there is a temporary picture of nephritis following salvarsan no permanent damage to the kidneys results. The above statement as to treatment in latent syphilis cannot be followed with a result in all cases. Some cases will become negative, others partly positive and some will have no effect from the treatment, judging from the Wassermann reaction. Charts I, II and III give an example of three types of latent syphilis we are treating, with the effect upon the Wassermann reaction.

CHART I.—LATENT SYPHILIS. DURATION UNKNOWN. FEMALE, AGED THIRTY-EIGHT YEARS.

Name—M. J.

Neo-arsphenamin.		Mercury salicylate.		Blood examination.		
Date.	Dose, gram.	Date.	Dose, grains.	Date.	Wassermann.	Hecht-Gradwohl.
June 24, 1921	0.6	Sept. 17, 1921	1	June 22, 1921	++++	++++
July 1, 1921	0.6	Sept. 24, 1921	1	July 1, 1921	++++	++++
July 8, 1921	0.6	Oct. 3, 1921	1	July 15, 1921	++++	++++
July 15, 1921	0.9	Oct. 10, 1921	1	July 29, 1921	++++	++++
July 22, 1921	0.9	Oct. 17, 1921	1½	Aug. 19, 1921	++++	++++
July 29, 1921	0.9	Oct. 24, 1921	1½	Sept. 28, 1921	++++	++++
Aug. 5, 1921	0.9	Oct. 31, 1921	1½	Oct. 6, 1921	++++	++++
Aug. 12, 1921	0.9	Nov. 7, 1921	1½	Oct. 25, 1921	++++	++++
Aug. 19, 1921	0.9	Nov. 14, 1921	2	Nov. 1, 1921	++++	++++
Sept. 14, 1921	0.9	Nov. 21, 1921	2	Nov. 15, 1921	++++	++++
Sept. 21, 1921	0.9	Nov. 28, 1921	2	Nov. 29, 1921	++++	++++
Sept. 28, 1921	0.9					
Oct. 6, 1921	0.9					
Oct. 13, 1921	0.9					
Oct. 20, 1921	0.9					

[3] Am. Jour. Med. Sc., July, 1921, No. 1, **162**, 80.

CHART II.—LATENT SYPHILIS. DURATION UNKNOWN. FEMALE, AGED THIRTY-TWO YEARS.

Name—F. S.

Neo-arsphenamin.		Mercury salicylate.		Blood examination.		
Date.	Dose, gram.	Date.	Dose, grains.	Date.	Wassermann.	Hecht-Gradwohl.
June 10, 1921	0.6	June 14, 1921	1	June 12, 1921	++++	++++
June 17, 1921	0.6	June 21, 1921	1	June 12, 1921	++++	++++
June 24, 1921	0.6	June 28, 1921	1	July 12, 1921	++++	++++
July 1, 1921	0.6	July 4, 1921	1	July 26, 1921	+++	++++
July 8, 1921	0.6	July 12, 1921	1	Aug. 15, 1921	+++	++++
July 15, 1921	0.9	July 19, 1921	1	Sept. 6, 1921	++	+++
July 22, 1921	0.9	July 26, 1921	1½	Sept. 14, 1921	++	+++
July 29, 1921	0.9	Aug. 9, 1921	1½	Sept. 27, 1921	++	+++
Aug. 5, 1921	0.9	Aug. 15, 1921	1½	Oct. 25, 1921	+	++
Aug. 11, 1921	0.9	Aug. 21, 1921	2	Nov. 29, 1921	+	++
Aug. 17, 1921	0.9	Sept. 6, 1921	2			
Aug. 26, 1921	0.9	Sept. 14, 1921	1			
Sept. 2, 1921	0.9	Sept. 20, 1921	1			
Sept. 9, 1921	0.9	Sept. 27, 1921	1			
Sept. 16, 1921	0.9					

CHART III.—LATENT SYPHILIS. DURATION UNKNOWN. FEMALE, AGED TWENTY-EIGHT YEARS.

Name—N. C.

Neo-arsphenamin.		Mercury salicylate.		Blood examination.		
Date.	Dose, gram.	Date.	Dose, grains.	Date.	Wassermann.	Hecht-Gradwohl.
Aug. 9, 1921	0.6	Oct. 3, 1921	1	Aug. 7, 1921	++++	++++
Aug. 16, 1921	0.6	Oct. 10, 1921	1	Aug. 16, 1921	++++	++++
Aug. 23, 1921	0.6	Oct. 17, 1921	1	Aug. 30, 1921	+++	++++
Aug. 30, 1921	0.6	Oct. 24, 1921	1	Sept. 14, 1921	++	++++
Sept. 7, 1921	0.6	Oct. 31, 1921	1½	Sept. 28, 1921	+	+++
Sept. 14, 1921	0.9	Nov. 7, 1921	1½	Oct. 12, 1921	+	++
Sept. 21, 1921	0.9	Nov. 14, 1921	1½	Oct. 19, 1921	Negative	++
Sept. 28, 1921	0.9	Nov. 21, 1921	2	Oct. 26, 1921	Negative	+
Oct. 5, 1921	0.9	Nov. 28, 1921	2	Nov. 9, 1921	Negative	Negative
Oct. 12, 1921	0.9	.....	....	Nov. 30, 1921	Negative	Negative
Oct. 19, 1921	0.9					
Oct. 26, 1921	0.9					
Nov. 2, 1921	0.6					
Nov. 9, 1921	0.6					
Nov. 16, 1921	0.6					

The medical literature is full of the different results which men get with different forms of salvarsan. Some make the statement that you get just as good if not better results and less reactions with the neo- preparation while others say the same about salvarsan.

I have used both and personally can find no difference from the effect upon the Wassermann reaction, although I do think the neo-preparation is more toxic in a number of cases. I am treating a woman at present with salvarsan who complains of no reaction, and after a small dose of neo-salvarsan she complained of intense itching over the body and sick stomach with vomiting, and in order to make sure that it was not caused by some physical condition present at that time, I gave another dose of the neo-salvarsan three weeks later and it had the same reaction. But in most cases there should be no difference between the two if administered and prepared properly. The neo-salvarsan is fast becoming popular, as it is very simple to administer and can be administered now with safety and result in 5 cc of distilled water. The following is the technic I use for salvarsan and neo-salvarsan: Double distilled water is used, the second distillation made in an all glass still. The water is distilled and autoclaved the afternoon before the morning treatments and the morning before the afternoon treatments. A separate flask is used for each patient, each flask containing about 200 cc 0.4 per cent sodium chloride. The flask is stoppered with gauze and capped with tin-foil. For some time past I have been using gauze in the place of cotton stoppers, as this does away with having fine particles of cotton fibers in suspension. Both the salvarsan and neo-salvarsan are given by gravity, the only difference is that more solution is used with salvarsan. For administering a regular glass graduated reservoir of 250 cc capacity is used, the end connected with a piece of rubber tubing, six inches long, to that a glass observation tube, and to that another piece of rubber tubing, eighteen to twenty-four inches long, the end of this connected with a Luer glass adapter. (If new rubber tubing is used, boil in distilled water and let soak overnight and rinse well before using.) I use a platinum needle, gauge 19, length one inch, and with this size I find no trouble in entering all size veins, and it is large enough to permit as rapid flow as one desires by gravity, the speed regulated by raising and lowering the reservoir. Into the reservoir place 100 cc 0.4 per cent sodium chloride solution; remove all air bubbles; apply tourniquet, and the instant blood appears in the glass adapter, release the tourniquet and at the same time let the fluid flow; after from 10 to 20 cc have gone from the reservoir and no tumefaction appears over the site of the injection, you are sure the vein has been entered properly and a good flow established. Now pour the solution of salvarsan or neo-salvarsan into the reservoir. If neo-salvarsan is used do not prepare the solution until you are sure the vein has been entered. I have seen reactions from the neo-salvarsan when it was prepared, and for reasons the vein was not entered and other veins had to be tried, and the time consumed was too long to leave the neo- preparation exposed to the air. When all the solution has passed from the

reservoir and through the observation tube the apparatus is lowered and a small quantity of blood runs back into the glass adapter and the needle immediately removed, at the same time pressing for a few moments over the site of injection to prevent the least amount of backflow from the vein. I see no advantage of using two glass reservoirs with an excess of parts nor the apparatus with the combined syringe attachment. With the above method one can get as rapid a flow as he desires, and there is no reason for forcing the solution into the vein.

The method of preparing patients for treatment is to give a saline laxative the night before and nothing to eat five hours before and five hours after injection. This is the ideal method and should be followed in all cases. But among our cases, due to the shortage of attendants and non-coöperation of the patients, it is not followed except in a few cases. However after administering over 700 doses we have had no effects which can be attributed to not carrying out the above precautions. Each patient is given a physical examination to determine the condition of the heart, bloodvessels, lungs, kidneys and liver. We have several cases of chronic nephritis and arteriosclerosis under treatment, and by carefully regulated dose and examinations of urine and heart we have had no untoward results.

Summary. 1. From our experience most cases of latent syphilis are not cured; but arrest in the development of the disease and comfort to the patient occur in a number of cases. The cases which show signs of improvement from a serologic standpoint can only be determined by treating and examining the blood.

2. Our results obtained from treating the syphilitic insane have more than compensated for the time and expense, and it is our plan to continue treatments.

3. It is a matter of individual opinion whether cases of general paralysis confined in institutions for the insane should or should not be treated. We have found no results obtained in such cases.

4. Every case in or out of an institution should have a spinal-fluid examination if the blood is positive.

5. Among 1500 cases examined for syphilis 12.5 per cent showed positive Wassermanns, and from this number of positive cases 26.2 per cent showed signs of neurosyphilis: 17.6 per cent being cases of general paralysis and 8.6 per cent other forms of neurosyphilis. It is to be remembered that the above examinations show the results from latent syphilis, as no case recorded in the above shows clinical signs of syphilis excepting the cases of paresis, and they of course belong in the tertiary stage as neurosyphilis.

6. In conclusion, I wish to emphasize the tremendous importance of the early discovery and proper treatment of syphilis and the examination of spinal fluids, and thus to lessen the number of incurable latent syphilis and neurosyphilitics.

THE ROENTGEN-RAY DIAGNOSIS OF TUBERCULOUS CERVICAL LYMPH GLANDS.*

By John Munn Hanford, M.D.,
NEW YORK.

In the course of a study of tuberculosis of the cervical glands the roentgen-ray method of diagnosis has served to differentiate it in some cases from Hodgkin's disease, lymphosarcoma, chronic lymphadenitis, carcinoma and cysts. The method has proved so useful as to appear to warrant a presentation of the findings.

From reading and observation one gains the impression that calcification in tuberculous glands of the neck has failed to attract its full share of attention. (1) It is said or implied by good authorities to be rare. (2) Its usefulness in diagnosis by the roentgen ray deserves emphasis.

In discussing tuberculosis of the superficial or external lymph glands, Holt, in *The Diseases of Infancy and Childhood*, states that "Calcification of the glands in this location is rare." *A Textbook of Pathology*, by MacCallum, in referring to tuberculosis of the lymph glands, fails to mention calcification in connection with the cervical glands, yet mentions it as occurring in tuberculous glands generally. From his text on the various groups one might readily conclude that calcification in the cervical lymph glands was not frequent. Adami and Nicholls in 1911, in *Principles of Pathology*, in discussing tuberculosis of the lymph glands, say, "In long-standing cases the glands . . . may contain calcareous spicules." Several recognized pathologists have recently told the writer that they had rarely seen it; and one said he had never seen it.

To contest these views on the rarity of calcification in tuberculous cervical glands the following evidence is presented:

Incident to a three and a half years' study of this disease, during which time some 200 cases have come under close observation and treatment, roentgen-ray plates of the neck of 40 unselected patients were made; 21, or 52.5 per cent of the forty plates, showed definite areas of increased density corresponding in location to the lesions found on physical examination. These areas of density are distinctly more marked than are the shadows of the soft parts. Indeed, they are almost of the density of bone (Fig. 1). They correspond in location to the enlarged glands, sinuses or cold abscesses. They vary in size from a birdshot to an almond; they may be single or multiple; and in two plates the appearance is that of a large area of fine sand (Fig. 2).

* Read before the Surgical Section of the New York Academy of Medicine, March 4, 1921.

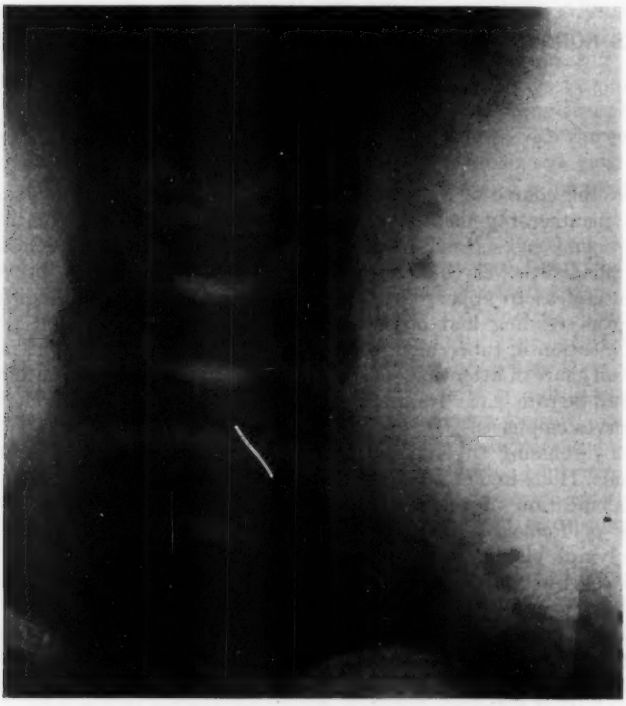


FIG. 1.—A marked example of calcified lymph glands.

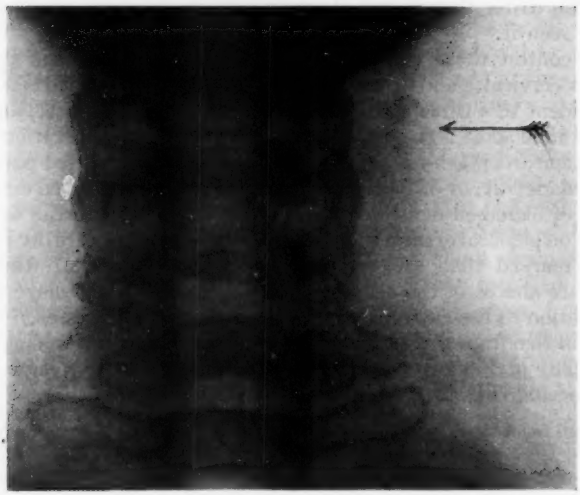


FIG. 2.

Of the 21 patients with positive plates, 10 were proved tuberculous by microscopic examination of tissue excised from the neck. All of the remaining 11 cases were clinically typical of tuberculous glands. Four of these showed such marked, large, discrete areas of density in the plates as to leave little argument about this diagnosis (Figs. 1 and 3). Three were clinically diagnosed in the Presbyterian Hospital tuberculosis clinic as pulmonary tuberculosis (which fact is strong presumptive evidence in favor of the glands being tuberculous). The remaining 4 presented cold abscesses from which typical caseous material was removed and which persisted subsequently as sinuses.

FIG. 3.—This patient had previously had in another hospital by a good surgeon, bilateral "radical" operations, the only patient showing bilateral shadows.

Of the 19 patients who showed no areas of increased density in plates of the neck, 14 were proven tuberculous by microscopic examination or by guinea-pig inoculation. Of the 5 others, 2 had definite pulmonary tuberculosis; 1 presented a cold abscess, caseous material and subsequent persistent sinus; 1 had had proved tuberculous peritonitis; and 1, though not furnishing other evidence, was a typical case clinically. It is the conviction of the writer that all of the 40 patients had tuberculosis of the cervical glands. The age of the patients ranged from five to forty-five years. By chance no younger children were included in the series.

The natural deduction is that the areas of increased density are due to lime salts—to calcification.[1] They have been so reported by the roentgenographic department of the Presbyterian Hospital. Calcification goes with necrosis, and is well known to be common in tuberculosis of the lung and of the mediastinal lymph glands.[2] Tuberculosis of the cervical glands is notorious for its necrosis. What other pathology than calcification incident to tuberculosis could throw these shadows?

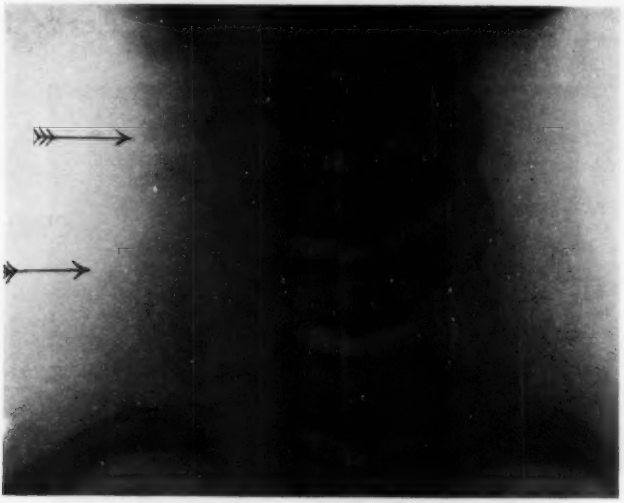


FIG. 4.—The lower arrow points to a small shadow corresponding exactly with the site of a small cold abscess. This girl was referred with the probable diagnosis of a branchial cyst.

In this study only a few plates were obtained of non-tuberculous lesions. None showed evidence of calcification. There was one remarkable case of Hodgkin's disease with extensive necrosis and ulceration in the neck of many months' duration which at autopsy showed no evidence of calcification.

In a study of the literature and in a wide personal canvass, simple lymphadenitis, Hodgkin's disease, lymphosarcoma, carcinoma, syphilis, cysts and fistulæ of the neck and other lesions that might be confused with tuberculosis here have not been shown to present calcification nor other changes revealing such increased density by the roentgen ray.[3] It is only fair to state certain exceptions acquired by the writer to this statement. MacCallum

[1] Opie, E. L.: The Focal Pulmonary Tuberculosis of Children and Adults, Jour. Exper. Med., June, 1917, 25, 855.

[2] Ibid.

[3] Substantiated by personal communication from Drs. Jobling, Longcope, Symmers Clarke and others.

describes calcification in adenomatous goiter and Le Wald cites instances of thyroid glands showing calcification by the roentgen ray. This would not readily be confused with disease of the lymph glands. In "Notes on Tumors," Wood says, "The contents . . . (of a dermoid cyst) . . . may undergo calcification." These are found, he says, "In the parotid region" and "in the deeper tissues of the lateral aspects of the neck." We know, however, that these locations are rare for dermoids, and we may infer that, even so, they do not frequently calcify. Dr. E. W. Peterson reported to the writer a personal case wherein the pathologist reported calcification in queer malignant tissue from a cervical lymph gland. Calcification of an artery in the neck might throw a confusing shadow, but most of our difficulty of diagnosis in cervical lymph-gland disease we meet in subjects too young for arteriosclerosis.

Four explanations are offered by the writer for the supposed rarity: (1) The lime salts are often thinly distributed in the periphery of the necrotic mass when seen microscopically as a blue layer but not noticeable on gross examination.[4] (2) In 2 of the writer's cases before operation the roentgen ray showed very definite shadows (Fig. 2) while at operation the site of the shadows was occupied by a large cold abscess with a thickened capsule. It is thought that the lime sand was suspended in the pus, like a fine emulsion, and therefore undetected. (3) The pathologists customarily and justifiably examine only one or two of a mass of excised tuberculous glands without searching through the whole. (4) The cervical glands are rarely examined at autopsy.

The 21 positive plates indicate that tuberculous disease of the cervical lymph glands may, beyond all reasonable doubt, give evidence of calcification, and, conversely, that the evidence of calcification, studied in conjunction with the clinical findings, spells tuberculosis.

The practical application of this relatively frequent occurrence at once becomes apparent, and indeed is recognized by individual workers here and there.[5] [6] Whatever the percentage of incidence, evidence of calcification is sufficiently frequent in patients with tuberculous lesions in the neck to warrant everyday use of the roentgen ray in diagnosis. It will often save a patient a biopsy which scars the neck, causes discomfort and necessitates some loss of working time.

One plate is so inexpensive as to make it worth a trial even though there is a good chance of its being negative. A small plate that fits between the occiput and the second dorsal vertebra, and snugly against the back of the neck, is more likely to pick up the smaller

[4] Symmers: Personal communication.

[5] Haynes, R. S.: The Differential Diagnosis of Enlargements of the Cervical Lymph Nodes, Arch. Pediat., New York, 1918, **35**, 226.

[6] Editorial: Standards of Diagnosis and Treatment of Tuberculous Cervical Adenitis, Am. Rev. Tubere., Baltimore, 1918–19, **2**, 564.

shadows than a larger plate. One anteroposterior view is usually sufficient. The lateral views are rarely helpful, unless there be lesions in the median line, because the glands are largely obscured by vertebræ, mandible, hyoid bone and thyroid cartilage. Except in children the usual chest plate is not long enough to ensure a good view of the chest and the neck.

Evidence of tuberculosis of glands.	21 patients showing shadows in plates.	Age.	Sex.	Number of chart.
Clinical and roentgen-ray plate	C. S.	30	F.	88307
	G. T.	12	F.	77277
	N. C.	45	F.	97803
	M. M.	48	F.	97958
Clinical and tuberculosis of the lungs	L. S.	30	M.	74349
	J. L.	11	F.	96321
	J. M.	26	M.	6947
Clinical, persistent sinus, necrotic material and the old history of excised tuberculous gland	T. G.	10	F.	71175
Clinical and persistent sinus	K. O'R.	16	F.	92284
	M. S.	6	F.	P. P.
	C. S.	27	M.	1551
Microscopic examination of the tissue excised from the lesion	E. U.	19	F.	43274
	M. B.	27	M.	46555
	S. P.	30	F.	43444
	E. S.	22	F.	45341
	G. P.	15	F.	48616
	S. T.	10	F.	45771
	H. H.	20	M.	2223
	C. B.	15	F.	1710
	J. M.	20	F.	1737
	H. C.	21	M.	P. P.
	19 patients showing no shadows.			
Clinical and proved tuberculosis of the peritoneum	J. McK.	10	F.	97662
Clinical and tuberculosis of the lungs	A. L.	5	F.	42608
	K. L.	26	F.	97804
Clinical	P. M.	28	M.	96052
Clinical and persistent sinus	S. G.	23	F.	73387
Microscopic examination of the tissue excised from the lesion or positive guinea-pig test of material from the lesion	M. K.	24	F.	92680
	F. K.	24	M.	89999
	M. H.	8	F.	44262
	A. N.	42	F.	35192
	H. Y.	22	M.	37842
	W. F.	23	M.	43265
	T. G.	28	M.	39434
	M. Z.	17	F.	22461
	M. F.	8	F.	93009
	M. R.	14	F.	P. P.
	S. D.	29	M.	2090
	C. W.	28	F.	34232
	F. S.	19	F.	1600
	J. A.	17	M.	49619

It is important to make a positive diagnosis of diseased cervical lymph glands. The treatment varies with the disease. Some cases of Hodgkin's disease and some of tuberculosis profit by therapeutic operative removal; but with a similar clinical picture in each the operation might not be the same. Likewise, and perhaps more important, if roentgen therapy be employed the dosage which, for example, may help to heal tuberculosis may indeed accelerate the advance of carcinoma, lymphosarcoma and Hodgkin's disease.

Conclusions. 1. Calcification in tuberculous cervical lymph glands is not rare. Although the series here presented is small, the indication is that calcification occurs in 52.5 per cent of such patients over five years of age.

2. A positive diagnosis of tuberculous cervical glands, abscesses and sinuses may be made so frequently by a small plate, studied with the clinical picture, as to render the roentgen ray worth a trial before subjecting the patient to a biopsy.

The writer acknowledges, with grateful appreciation, the assistance given to this study by the College of Physicians and Surgeons, Columbia University, through the Bull and the Harriman fellowship funds.

THREE CASES OF LEUKEMIA IN ONE FAMILY.*

By Charles W. McGavran, M.D.,

Formerly Professor of Clinical Medicine, College of Medicine, Ohio State University; Physician to Grant Hospital, Columbus, Ohio.

These cases are reported not because they present unusual clinical features as leukemia, but because of the interesting facts that three members of one family were affected, and of the most unusual combination, there being one of the myelogenous and two of the lymphatic type.

While there are those who hold that leukemia is of bacterial origin and others that it follows infectious processes of long duration, *i. e.*, tuberculosis, syphilis and malaria, and still others that it is due to a new growth of the blood-forming tissues, yet the fact remains that the etiology of leukemia is unknown. We have no evidence that would prove that heredity is a factor in this disease, although some authors have advanced such a theory. Nor has evidence been produced that would cause one to believe that it is transmitted from man to man.

* Reported to the Columbus Academy of Medicine, November 14, 1921.

Ward[1] has accumulated valuable data as to the familial instance of leukemia, and in his analysis of 1457 cases speaks of Cameron's[2] cases, which were probably acholuric jaundice, and quoting from Ward as abstracted by Tyce, *Practice of Medicine:* "Ward quotes Obrastzow's[3] cases, in which a boy who had acute leukemia was nursed by a male nurse who later developed the same type of leukemia; and Bie's[4] case in which the father of a family died of chronic myelemia, and just before his death a servant girl fell ill of the same disease. Dock's observation[5] of myelemia in a mother whose daughter later developed the same and whose husband developed splenic anemia one year after his wife's death is also referred to."

In the whole series there are two possible instances of familial cases: Jewett[6] had under his care a girl, aged seven months, with acute myelemia. He states: "It seems highly probable from the history that a brother and a sister of this child also died of leukemia. The eldest brother at the age of five months developed enlargement of the abdomen and great anemia. He died six months later. The sister at four months developed marked anemia, splenic tumor and emaciation. She died at eight months. Mother and father are alive and well."

Ward remarks that this report is suspicious on the face of it. Leukemia at so early an age very rarely, if ever, manifests itself first by a splenic tumor, but rather by swollen glands, purpura, etc. These were probably cases of Gaucher's disease. Campbell[7] reported that he knew of a woman under treatment for leukemia whose white cells fell from 400,000 to 5000 after five months' treatment, and adds, 'Her child was under treatment for leukemia at the same time.' There are no further details. Hancsel[8] reports "acute leukemia in a boy whose uncle was also suffering from the disease. The diagnosis appears to have been quite satisfactorily established, but there is nothing to indicate that it was more than a coincidence."

Ward finds that males are more frequently attacked than females and that each of the three forms has an "age of election." Acute leukemia, occurs more frequently up until the twenty-fifth year and has its highest peak during the first five years; chronic myelogenous leukemia is more prevalent between the ages of

[1] Jordon: The Infective Theory of Acute Leukemia, British Jour. Infect. Dis., January-March, 1917, **14**, 10.
[2] Am. Jour. Med. Sc., 1888, **95**, 28.
[3] Deutsch. med. Wchnschr., 1890, **91**, 1150.
[4] Ugeskr. f. Laeger, 1910, **74**, 1607.
[5] Am. Jour. Med. Sci., 1904, **127**, 563.
[6] Philadelphia Med. Jour., 1901, **17**, 816.
[7] Lancet, 1912, vol. **1**, p. 1473.
[8] Wien. klin. Wchnschr., 1908, **21**, 594.

twenty-five and forty-five years, while chronic lymphatic leukemia more often occurs between the forty-fifth and sixtieth years.

The cause of leukemia being unknown, no opinion will be ventured as to why three male members of the same family were affected with this disease. The author is fully aware that no case report is complete without an autopsy, and particularly that a diagnosis of leukemia is not complete without the pathologic findings of the blood-forming tissues. Two of these cases were under the observation of the author at the same time, and are reported in detail, showing the clinical work that led to the diagnosis.

On July 6, 1920, S. S. L., aged fifty-nine years, a stonemason, complaining of headache, nausea and vomiting, was seen in consultation with Dr. T.

Family History. Father died at eighty-three years of age; mother living, eighty years of age and healthy. There were four brothers—one brother living and healthy at thirty-five; one died at forty of epilepsy; one died at forty of leukemia; one died in childhood, cause unknown. There were five sisters—two are living and well, aged thirty-six and forty respectively; three sisters dead: one died at fifty-eight of tuberculosis, one died at forty-three (cause unknown) and one died at thirty of tuberculosis.

Patient is married (wife is healthy, the mother of four healthy children, and has not miscarried); he has had no previous serious illness. Three years ago he noticed a dry scaly condition on the right side of the face about the size of a nickel. This was diagnosed cancer by Dr. S., who treated it with the roentgen ray every week for a year, but with no improvement. He then consulted Dr. X., who used paste; by this time he had sores on both sides of the face, the lower lobe of the right ear being involved. His face healed promptly after the use of paste, leaving large scars. Since that time until two weeks ago he has been working at his trade. Two weeks ago he began to feel sick, paroxysmal frontal headaches coming specially at night; at about the same time he began to have nausea and vomiting, and has retained little food. His physician found several infected teeth, which have been extracted. His headaches have progressively increased in severity. Today he is delirious.

Physical Examination. "Patient is poorly nourished; muscles of good tone. Hair thin and gray; scalp shows considerable seborrhea. Pupils equal, react promptly to light and distance. Mucous membranes somewhat under color. Patient is confused; seems to see all right but cannot answer questions intelligently. Tongue is coated; teeth chewing-surface poor; gums sore from recent extraction; tonsils cryptic and show evidence of infection; large stellate scars on each side of the face; lobe of the right ear is

deformed; all the superficial glands (submaxillary, cervical, post-cervical, axillary and inguinal) are palpable; they vary in size from an acorn to that of a walnut; they are freely movable and not tender; the radial pulses are equal, regular as to force and frequency, of low tension and easily compressible; blood-pressure, 110/68; the chest and vertebral column are negative; heart and lungs show nothing remarkable; examination of the abdomen is quite unsatisfactory, owing to the extreme muscular rigidity and the mental condition of our patient; he not only does not assist in the examination but moves from side to side, making a satisfactory examination impossible; the abdomen is distended; the area of splenic dulness is increased, but its actual size is not determined; the knee-jerks are preserved.

Discussion. "A very interesting case and one worthy of complete clinical study. Should the glandular involvement be a metastasis from the face, and if the face lesion was a cancer, the prognosis is hopeless. We must not, however, overlook the possibility of lymphatic leukemia or syphilis. Will examine blood, urine and make a Wassermann."

July 7, 1920. Whites, 162,000; lymphocytes, 95; small lymphocytes predominating cell; only moderate number of smudges.

July 7, 1920. Urine: amber; acid; albumin, very slight trace; sugar negative; microscopic: moderate number of red blood cells with occasional pus cell; no casts.

July 8, 1920. Hemoglobin, 80; reds, 4,000,000; whites, 170,000; smears show the same picture as before.

July 8, 1920. Wassermann negative.

July 8, 1920. Diagnosis of lymphatic leukemia is made. Benzol, gr. seven, in capsules t. i. d., and sodium cacodylate, gr. six, intravenously every third day, were recommended

July 20, 1920. Reds, 4,100,000; whites, 98,500; blood picture shows no change except fewer cells; reds are normal in appearance.

July 31, 1920. Hemoglobin, 80; reds, 3,520,000; whites, 65,000; polynuclears, 2; lymphocytes, 98.

While there was a reduction in the number of white cells following the administration of benzol and arsenic there was no improvement in the patient; he gradually became more toxic and died during the first week of August. Autopsy, although greatly urged, was absolutely refused.

July 8, patient's son came to the office and was told of the diagnosis and the grave prognosis. Among other things the author said: "While your father's blood count is high, it does not compare with that of the patient who just left the room before you entered. While your father has a leukocyte count of 162,000, that man came here four months ago and we found a leukocyte count of over 300,000." "Why, doctor! that man is my father's uncle."

I. C. L., male; married; aged sixty-nine years, farm superintendent, was first seen February 17, 1920.

Complaint. Shortness of breath and precordial pain upon exertion.

Family History. Father died at sixty-three of apoplexy; mother died at seventy-one years of age; there were six brothers: one living and well at eighty; five dead—one died at forty-five of epilepsy; one died at fifty of epilepsy; one died at eight-two years of age; one died at seventy-one of heart disease; one died at seventy-six of heart disease. One sister living and well at seventy-seven; one sister died at sixty-eight, cause unknown.

Present History. Has been a fairly healthy man. Has never had any serious illness. Has lived a life of exposure. Has been subject to frequent colds. For the past fifteen years has had frequent attacks of "catarrh" of the bowels, manifested by abdominal pain and diarrhea. Prior to six years ago had attacks of severe epigastric colicky pain. For the past three years has had shortness of breath and precordial pain upon exertion, gradually becoming more severe. These pains are precordial and radiate up the sternum and down the arms, especially the left. He at times perspires freely, during and after these attacks, and has a feeling of depression and great anxiety. For the past three years has had more or less ringing in the ears. Has no headache. Vision is not disturbed. Appetite is good; eats everything; now masticates well, although until two years ago he was without teeth for twelve years. Bowels are regular; he is a good sleeper; formerly weighed 155 to 160 pounds, but one year ago lost to about 135 pounds. Today weighs 132½ pounds. Kidneys act freely; nocturia one to three times.

Physical Examination. Patient is poorly nourished; muscles of fair tone. Hair gray; scalp in fair condition. Temporal arteries are tortuous; advanced arcus senilis. Pupils equal; react promptly to light and distance. Mucous membranes under color. No marked obstruction to nasal breathing. Tongue is slightly coated; teeth artificial above and below; fauces somewhat injected; tonsils cryptic and show evidence of past inflammation; thyroid negative; the postcervical, axillary, epitrochlear and inguinal glands are distinctly palpable, varying in size from that of a pea to a hickory-nut; they are freely movable and not tender; the larger glands are found in the inguinal region; radial pulses are equal (76), regular as to force and frequency, not of high tension, easily compressible; radial arteries are just palpable; brachials are distinctly palpable and tortuous; blood-pressure, 148/74. Chest is symmetrical; vertebral column negative; decided pulsation in episternal notch; percussion of the chest is negative, cardiac dulness being 11 cm. to the left and 3 cm. to the right of the midsternal line on a level

with the fifth interspace, being 7 cm. at the junction of the third costal cartilage with the sternum. Breath sounds are clear except for many indeterminate rales scattered throughout the chest. Heart tones are clear but metallic. There is a decided cardiovesicular murmur just over the second left rib. Abdominal examination shows a left inguinal hernia, for which patient is wearing a truss. There is tenderness in the epigastrium. Lower border of the stomach three finger-breadths below the umbilicus—patient in recumbent posture—lower border of liver one finger-breadth below the costal margin; in the midline there is an area of dulness which is probably the liver, extending four finger-breadths below the ensiform appendix. Area of splenic dulness greatly increased. Lower border of spleen distinctly palpable four finger-breadths below the costal margin. Unable to palpate either kidney. The prostate is not specially tender; is hard and nodular.

Discussion. The history of this case is quite typical of coronary sclerosis. It is specially interesting in view of the low blood-pressure. The interesting things brought out in the examination are the involvement of superficial glands together with the enlarged spleen and the general prostatic hypertrophy. Will make the complete clinicals.

February 17, 1920. Hemoglobin, 70; reds, 3,380,000; whites, 330,000; differential; polynuclears, 3; lymphocytes, 95; mononuclears, 2. This is a case of lymphoid leukemia. The predominating cell is the small lymphocyte, although there are a few large and intermediate forms; only a few smudges; the reds show no variation of shape or size. They have a slight washed-out appearance.

February 17, 1920. Urine: specific gravity, 1020; sugar, negative; albumin, slight trace; microscopic: very occasional hyaline cast.

February 18, 1920. Urine, twenty-four hour specimen: 700 cc; specific gravity, 1022; albumin, very faint trace; sugar negative; microscopic: no red blood cells; no casts nor pus cells found. Blood: Whites, 378,000; differential same as reported above. Feces: Formed; dark brown in color; occult blood negative; microscopic: shows no undigested meat fibers; no increase in fat; no parasitic ova.

February 18, 1920. *Fluoroscopic Examination of Chest and Abdomen.* Barium meal shows stomach to be normal in position and contour; definition not good; peristalsis normal; duodenal cap shows no irregularity. There are dense areas beneath the diaphragm on both the right and the left of the stomach. Heart shows nothing remarkable. There is an increase of mediastinal tissue, but this is not marked. In six hours the stomach is empty. Head of the meal in ascending colon; in thirty hours the entire colon is visualized and shows nothing remarkable.

February 19, 1920. *Diagnosis.* Lymphatic leukemia with coronary sclerosis and prostatic hypertrophy. The prognosis is not good.

Patient was advised to rest and was given three injections of arsphenamin in 0.3 gm. doses at intervals of two weeks. At first there seemed to be some improvement; the patient said he felt stronger, and the spleen on March 17 was smaller, being 3 cm. below the costal margin. There was only a slight reduction in the white count. Following the third injection of arsphenamin on March 17 there was a severe reaction and the patient reported on April 14, saying that since he was resting he has had no precordial pain, but that he now felt quite weak. He weighed 131 pounds; spleen was larger than when he first presented himself and a definite increase in size of all superficial glands. His blood showed 400,000 whites, over 98 per cent being lymphocytes, the great majority of which were small.

He was then placed on benzol, gtt. vij, in capsules after each meal, and was sent home with a letter to his family physician, Dr. S., advising that he be given sodium cacodylate, gr. iij, intravenously, twice a week.

On May 21 the patient returned, saying he felt much stronger. But other than a reduction in the number of the white cells there was no change in his condition; the count showed 144,000 whites; smear shows the percentage of lymphocytes to be about the same; more smudges than in former slides.

On July 7 examination showed no change clinically; blood: hemoglobin, 75 per cent; whites, 198,000; differential unchanged.

On September 1 the patient says he has been working every day, has had no precordial pain and very little shortness of breath; feels much stronger. Blood: Hemoglobin, 85 per cent; whites, 98,000; differential unchanged. The author's remarks on patient's case record on that date were as follows: "The spleen, liver and superficial glands remain unchanged in size. Patient seems stronger, and as long as he improves under benzol and sodium cacodylate will not recommend radium, although should there be an increase in the number of lymphocytes I will at once advise use of radium."

On November 8 the patient returned, saying he felt better, although two weeks before he had a severe attack of neuralgia of the heart, lasting over three hours and requiring a hypodermic of morphin (this was angina). He looks more pale, otherwise no change in his condition. Weight today, 124½ pounds. Blood: Hemoglobin, 75 per cent; reds, 2,500,000; whites, 54,000; smear shows about the same differential, a thin smear giving many smudges; red cells show no irregularities as to shape and size.

It is to be noted that while the patient thinks he is better, the

only change that might be considered as an improvement is the reduction in the number of lymphocytes, in which there has been a notable drop. On the other hand he is more anemic and continues to lose in weight.

A letter from Dr. S., stated that on November 13 the patient became toxic and died on November 20, and that no autopsy had been held.

The son then said, "Five years ago my uncle, W. G. L., died of some blood disease; he was treated by Dr. H. M. Brundage."

Dr. Brundage reports as follows: "I examined my records carefully and can only find the enclosed blood count in the case of Mr. W. G. L. I saw him at the request of Dr. H. The blood count, you will notice, is significant of splenomyelogenous leukemia. I gave him every possible treatment from benzol to the roentgen ray, and even salvarsan was administered. He requested that at his death I should make a postmortem, which, as I remember, did not reveal anything extraordinary outside of a very large spleen."

Clinical report of Dr. Brundage: "Hemoglobin, 78; erythrocytes, 4,616,000; leukocytes, 213,000; polynuclears, 55; small lymphocytes, 4; large lymphocytes, 3; mast cells, 4; neutrophilic myelocytes, 33; eosin, 1. H. M. BRUNDAGE, M.D."

Our great regret is that an autopsy in the case of S. C. L. was absolutely refused. In view of the lack of pathologic evidence these cases are reported at length in order to strengthen the claim of a diagnosis of leukemia.

W. G. L., as reported by Dr. B., and who died of myelogenous leukemia, and S. C. L., who died of lymphatic leukemia, were brothers, and I. C. L., who also died of lymphatic leukemia, was their uncle, being their father's brother.

This family has certainly been "hard hit," for you will observe that in addition to the leukemia there were 3 cases of epilepsy, 2 in the branch I. C. L. and 1 in that of S. S. L. There were also 2 known deaths from tuberculosis in the branch of S. S. L. and 1 doubtful case in the family of I. C. L.

The author does not wish to be understood as trying to strengthen the claim of heredity as a factor in leukemia. He has endeavored to establish the diagnosis of leukemia and to report these cases as a most unusual coincidence. Dr. James H. Warren, associated with the author, has done all the laboratory and fluoroscopic work, and much credit is due him.

THE CLINICAL SIGNIFICANCE OF TOTAL AND DIFFERENTIAL LEUKOCYTE COUNTS, WITH SPECIAL REFERENCE TO ACUTE INFECTIONS.*

By Walter Clinton Jones, M.D.

DIRECTOR, PATHOLOGICAL DEPARTMENT, ST. VINCENT'S HOSPITAL, BIRMINGHAM, ALABAMA,

AND

Clara Enerie Brown,

BIRMINGHAM, ALABAMA.

(From the Pathological Department of South Highlands Infirmary, Birmingham, Alabama.)

After a thorough review of the extensive literature on this subject, we have formulated the following brief conclusions as being especially pertinent to the theme in hand.

I. **Total White Count and Percentage of Polymorphonuclears.** (1) The majority of writers agree that in most acute infections the total number of leukocytes in the blood is a measure of the patient's resistance and that the percentage of polymorphonuclears is an index of the severity of the inflammation. To Sondern[1] very largely belongs the credit of establishing these two all important principles. (2) Some authorities rely mostly on the total count, while others depend more on the percentage of polymorphs; but reliance on either to the exclusion of the other is frequently misleading. Of the two, however, the differential count probably has the greater value; but neither should be omitted in any critical case.

II. **Lymphocytes.** (1) Reduction in the number of lymphocytes below normal, especially below the normal number per cubic millimeter, is an unfavorable development; and an increase in their number, if not too excessive, is a favorable prognostic point. This conclusion seems to have been reached especially in tuberculosis, but it most likely applies also to various other diseases both acute and chronic. (2) The significance of an increase or a decrease in the number of small lymphocytes alone or of the large ones exclusively, does not seem to be understood.

* Read before a joint meeting of the Birmingham Pathological Society and the attending staff of South Highlands Infirmary, February 11, 1921.

[1] The Present Attitude of Blood Examination for Diagnostic Purposes, Boston Med. and Surg. Jour., 1905, **153**, 690–692. Idem, The Present Status of Blood Examination in Surgical Diagnosis, Med. Rec., 1905, **67**, 452–455. Idem, Value of the Blood Count in Sepsis, New York Med. Jour., 1906, **83**, 1245–1246. Idem, The Value of the Differential Leukocyte Count in Gynecology and Abdominal Surgery, Med. Rec., 1906, **70**, 989–990. Idem, The Value of the Differential Leukocyte Count in Diagnosis, Am. Jour. Med. Sc., 1906, **132**, 889–891.

III. **Indexes of Body Resistance.** Several of these have been orginated by various workers in this field. That of Walker's[2] we think is the best. It is computed in the following manner: He takes 10,000 as the highest possible normal total leukocyte count and 70 as the greatest possible normal polymorphonuclear percentage. For each rise of 1 per cent of the polymorphonuclears above 70 there should be an increase in the total count of 1000 above 10,000. Thus if the polymorphonuclear percentage is 80 (10 above 70) the total count should be 20,000 (10,000 above 10,000), in order to make the index normal, or zero. If in this instance the total should rise to 25,000, the index would be +5; if to 30,000, +10, etc. On the other hand, still assuming the polymorphonuclears to be 80 per cent, if the total leukocytes were only 15,000 they would be 5000 lower than they should be, making an index of −5; if they were only 10,000 the index would be −10, etc. In the cases of pneumonia, influenza, measles and empyema, which Walker cites, the index nearly always is positive if the disease is progressing favorably; negative, if it is serious; and invariably negative in all fatal cases.

IV. **Miscellaneous Data.** Ether anesthesia, operative trauma, moderate shock, moderate hemorrhage, physical exercise, reclining posture, short cold baths, pregnancy, normal digestion, diurnal factors, geographic location, elevation and personal idiosyncrasies usually cause more or less increase in the total white count.

Personal Investigations. This description of our work is in the nature of a report preliminary to further efforts along these lines. Although our conclusions are, we think, in the main correct, yet they are to some extent tentative, because knowledge in this field of hematology is by no means complete at present.

Our counts were made by means of a Levy counting chamber with Neubauer rulings. Two hundred or three hundred cells were enumerated each time. The blood samples were taken at various times of the day; it usually was impracticable to get them the same hour each day when two or more counts were made on the same individual. From one to fifteen counts were made on each patient, at intervals varying from six hours to twenty-four days.

Wright's stain was used, although we were fully aware of the fact that some specialists in this field do not hold it in high esteem. As far as we are concerned, we feel very grateful to Wright for devising his stain, for without rapidity of method thus made possible we would have been unable to obtain sufficient time from our busy routine to make the examinations which form the basis of this article. While Wright's stain does not bring out all cytologic details that every hematologic investigation requires, yet it was

[2] An Index of Body Resistance in Acute Inflammatory Processes, Jour. Am. Med. Assn., 1919, **82**, 1453–1457.

ample for our purpose, for we needed a stain which would enable us merely to distinguish polymorphonuclears from lymphocytes and also differentiate these two groups from the various other commoner varieties. Wright's stain when rightly handled accomplishes these results satisfactorily.

Our counts were made on patients suffering from the following diseases: 21 cases of appendicitis ranging in severity from very mild to fatally severe; 2 cases of puerperal infection; 2 secondary infections of laparotomy wounds; 1 each of the following: abscess of the kidney; abscess of retroperitoneal sarcoma; pelvic abscess following radium treatment; abscess of the lung following traumatic infection of the arm; abscess of tooth; acute pelvic gynecologic infection (?); eclampsia; postpneumonic empyema; cyst of spleen; acute lobar pneumonia; infection and gangrene of ovarian cyst complicating pregnancy; chronic salpingitis and retroflexion of uterus; recurrent pyelitis with salpingitis (?); chronic cholecystitis; nephroptosis; incomplete intestinal obstruction; mucous colitis; pyelonephritis; mild cerebral hemorrhage; posttyphoid lumbago; uterine hemorrhage, chronic cervicitis, and retrodisplacement of uterus; myocarditis, endocarditis, and appendicitis (?); one undiagnosed case. All of above patients except 4 were occupants of South Highlands Infirmary.

We will discuss our cases in regard to the hematologic principles we wish to elucidate rather than according to the various kinds of inflammatory diseases we have investigated, for in the class of infections considered in this report we found these principles to be practically the same, regardless of the nature of the invading bacteria or the portion of the body attacked.

General Explanation of Figures. The total leukocyte count was obtained according to the usual method. The percentage of polymorphonuclears was ascertained by the ordinary procedure of counting spreads on slides. The total polymorphonuclears per cubic millimeter was computed by multiplying the total count by the percentage of polymorphonuclears. Walker's index was worked out according to the method already described (p. 554). The total number of lymphocytes per cubic millimeter was obtained by multiplying the total leukocytes by the percentage of lymphocytes (taken from the differential count).

The line in the upper portion of each figure extending to the right on a level with "10,000" indicates the highest possible normal number of total leukocytes. The first line below this designates 7000 as the highest possible normal total number of polymorphonuclears. The line on a level with "70" signifies the highest normal percentage of polymorphonuclears. The line to the right from "zero" denotes normal resistance according to Walker's index. The lowest line on the right side indicates 1000 as the lowest possible normal number of lymphocytes per cubic millimeter.

The vertical columns of arabic numerals are arranged so that exactly the same amount of vertical space is allowed for a change of 1000 in the total leukocytes or total polymorphonuclears, for a variation of 1 per cent in the percentage of polymorphonuclears, and for a shifting of one point in Walker's index. The vertical intervals under "Total Lymphocytes" have no definite relations like those just described.

1. **Total Leukocyte Count.** Many if not the majority of clinicians look upon a rise of the total leukocyte count above normal in most acute inflammatory diseases as one of the indications of the presence of infection, and consider that a fall back toward normal means an improvement in the patient's condition; also, that the severity of the process corresponds fairly closely with the degree of the leukocytosis and the range of its fluctuations. The first point to stress in this connection is that the total count often is of little value in estimating the state of the patient. In fact, it may be positively misleading. For example, in Fig. 4, the fall of the total count from November 11 to 19 marks an exacerbation of the patient's infection. In Fig. 2 note that throughout the illness there was relatively little change in the total count and that it fell only from 16,000 to 11,000, a drop not corresponding clinically to the patient's prompt recovery from the operation. In Fig. 6 notice the decline of the total count from June 12 to 17, which parallels a marked aggravation of the patient's condition; the decided rise June 20 to 21 coincides with a very marked clinical improvement. Fig. 5, a fatal case, shows a gradual descent of the total count during the sixteen days immediately preceding the patient's death. This independent behavior of the leukocytic count occurs so frequently that by following along the rises and falls of the leukocytes from count to count one can find in every figure of this paper from one to five instances in which the total number of leukocytes either (1) rises with an improvement in the patient's condition or (2) falls with an exacerbation of the infection or (3) remains practically stationary while the clinical course either improves or gets worse—all three of these combinations being contrary to the significance commonly assigned by clinicians to the total leukocyte count.

On the other hand in many if not most instances the *general trend* of the total leukocytes does go hand-in-hand with the clinical course. Refer to Fig. 1, where the general direction of the leukocytic curve is downward while the patient at the same time makes a good recovery. This parallelism does not hold true, however, if one considers details too closely, for the drops from September 29 to August 1 and from August 3 to 4 were accompanied by aggravations of the patient's infection. But the general direction of the line does point toward the excellent recovery which the patient made. Figs. 2, 3, 4 and 6 illustrate cases precisely similar to the

one just described. Note also in a fatal case, Fig. 5, that the general course is downward, but not as markedly so as in the cases which recovered.

The most outstanding fact to be observed concerning the clinical significance of the total number of leukocytes is that they constitute the chief hematologic manifestation of the amount of resistance the body is making against the invading organisms. It is always a bad sign for the total leukocytes to register low unless the percentage of polymorphonuclears is correspondingly small. If the latter are high and the total leukocytes are low this combination means that a poor resistance is being offered against a severe inflammation—a situation which must be corrected if the patient is to recover. (See Fig. 5, September 24; this patient died. Compare Fig. 2, June 27, and Fig. 6, June 18 and 20.)

2. **Total Polymorphonuclear Count.** This parallels closely the total leukocytes. In comparing the two lines it is seen that they almost invariably lie relatively close together when the patient's condition is more or less serious, and separate from each other with clinical improvement. In Fig. 1, September 29, the patient's resistance is good and the two lines lie well apart; by October 1, the resistance had decreased markedly and the lines are twice as close together. On October 3 there was a decided improvement in the resistance and the lines at once separate from each other. In Fig. 6 note how close these lines lie to each other June 18 when the patient is at her worst, and how they gradually diverge as she recovers. All of the figures accompanying this article illustrate this principle very well. The approach and the spread of these two lines in relation to each other is an entirely new discovery of the senior author, and taken alone, independent of other hematologic findings, it constitutes an excellant guide to the patient's true clinical state.

3. **Percentage of Polymorphonuclears.** Of all the elements of a leukocyte count this probably is the most valuable. If these run high they mean a severe inflammation which usually, but not always, is purulent or gangrenous or both; and if the patient is to recover, relief must be obtained either spontaneously or by artificial means.

We would like to emphasize at this point the futility of trying to foretell with certainty whether pus is present by the degree of polynucleosis. (See Tables 1 and 2, which show that pus was found in the lesions with percentages of polymorphonuclears ranging from 64 to 94, and that pus was absent with percentages of 64 to 93.) But whether there be pus and gangrene or not a high polymorphonulcear count means practically without fail a severe inflammation or a marked toxemia of some kind. The nature of the invading bacteria very likely plays a part in this respect. Thus we know that certain streptococci may produce a

severe inflammation and marked toxemia with but little or no purulent exudate. On the other hand, bacteria of low virulence, like many strains of colon bacilli, may produce large abscesses with so little toxemia that there is no reaction on the part of the blood. Again, the infection may be virulent but the patient fails to put up a fight; in this case the blood is negative. Finally, the infected area may be so thoroughly walled off that there is no absorption of toxins and hence no hematologic response.

From a practical standpoint, however, the problem of diagnosis usually is solved sufficiently to determine an effective mode of procedure by correlating the blood findings with the clinical history and the physical examination. In this connection one must remember that high counts are of greater value than low ones in making a positive diagnosis, unless the latter follow the former. For example, in Fig. 4 a drop in the polymorphonuclears from 88 per cent to 68 per cent from November 29 to December 18 can mean but one thing, namely, a marked improvement in the pathologic process. The successive drops in Fig. 6, June 18 to 25, have exactly the same significance. The opposite sequence of a high following a low percentage has precisely the opposite meaning and can be relied upon implicity. (Refer to Fig. 5, September 21 and 24, and Fig. 6, June 17 and 18.)

4. **Polymorphonuclear (Walker's) Index of Body Resistance.** The nature of this index and the method of its computation have already been explained. We have been able to verify practically every claim that Walker makes for it. Minor fluctuations, as one might expect, frequently seem to have no clinical significance. However, in practically every case of ours that terminated favorably the index ascended well above normal (zero) and many times very far above it. (See Figs. 1, 2, 4 and 6, where the rises at recovery were only a moderate distance above zero.) In these patients recuperation was satisfactory but not as prompt and complete as in the case illustrated in Fig. 3, where the index rose enormously above normal. The case shown in Fig. 5, which ended fatally, had a very low index, never attaining normal.

Caution should be exercised in interpreting Walker's index when on or near the zero line except in connection with the percentage of polymorphonuclears. While in patients that have practically recovered the index may be at or near normal, the same is also true frequently of those suffering severe inflammations. For example, in Fig. 4, December 18, the index is approximately at zero, the total and polymorphonuclear counts are within normal limits and the patient has overcome almost completely her very severe infection. Now compare Fig. 6, June 12, P.M., when also Walker's index is at zero but the polymorphonuclears are at 88 per cent. The following morning the index has dropped to six below normal, and laparotomy the same day revealed an infected

gangrenous ovarian cyst. Compare again two more cases: in Fig. 1, October 18, the index is near the zero line (slightly above), the total leukocytes and the percentage of polymorphonuclears are practically normal and the patient has almost completed a clinical recovery. Compare Fig. 3, January 17, where the index also is approximately the same but the patient's polynuclears are 82 per cent, and he is very ill, suffering from a severe toxemia. The importance of always evaluating a normal Walker's index in connection with the percentage of polymorphonuclears may be better appreciated by likening a normal index accompanied by a normal polymorphonuclear count to a good dam with normal water-pressure behind it. No questions are asked; no fears arise. On the other hand normal index with a high polymorphonuclear percentage is like the same dam with a high water-pressure back of it. The question is asked at once, will the dam hold the flood? And one may fear the consequences if the structures should break. Similarily, if a patient's index is normal and his polymorphonuclears are high, one seeks to estimate whether the patient will be able to maintain his resistance and what the consequences will be if he fails.

Of course what one dreads most of all are marked depressions in the index caused by a high polymorphonuclear percentage and a low total leukocyte. (See Fig. 1, October 2; Fig. 2, June 27; Fig. 3, January 20; Fig. 5, September 24 and 27; and Fig. 6, June 18 and 20.) If a patient does not recover with reasonable promptness from such low readings as these he is almost sure to suffer dire consequences.

5. **Total Number of Lymphocytes per Cubic Millimeter.** These were computed by multiplying the total leukocyte count by the percentage of lymphocytes. Three features are particularly outstanding in regard to the total lymphocyte count:

Taken by itself it constitutes a very reliable index to the patient's condition. The lymphocytes almost invariably increase with the patient's improvement and decrease when the infection is worse; and they always rise high when recovery has become complete. Every figure in this article illustrates this point. In fatal cases the total lymphocytes remain close to or below lowest normal (1000). (See Fig. 5.)

The second point of interest is the discovery the senior author has made that the total lymphocyte curve parallels almost exactly the polymorphonuclear (Walker's) index of resistance. Every figure shows this feature. Why in rare instances (*e. g.*, Fig. 3, February 1 to 5) they run in opposite direction we are as yet unable to explain.

Concerning the relation of the total lymphocytes to the total leukocytes and to the percentage of polymorphonuclears, practically the same can be said that was stated in connection with the

polymorphonuclear (Walker's) index. The points to be noted are as follows: (*a*) A low lymphocyte count with a low or only moderately high percentage of polymorphonuclears is not a bad sign; and if at the same time the total leukocytes are high the outlook is favorable. (See Fig. 1, October 3 and 4.) This combination of low lymphocytes and low percentage of polymorphonuclears does not occur often, because when the percentage of polynuclears goes down the number of lymphocytes per cubic millimeter usually (but not always) increases reciprocally. (*b*) A low total lymphocyte enumeration with a high percentage of polymorphonuclears and a high total leukocyte count indicates a more or less serious condition. This is the most frequent combination found. (Refer to Fig. 4, November 11; and Fig. 6, June 12.) (*c*) A low total lymphocyte count with a low or only moderately high total leukocyte count and a high percentage of polymorphonuclears constitute a combination which signifies a very serious state that frequently ends fatally. This situation is encountered in a rather small percentage of patients. (See Fig. 4, November 19 to 29, and Fig. 5, September 24) [a fatal case].

6. **Correlation with Clinical Findings.** An extensive blood picture as described above has its final significance only when evaluated in connection with the clinical history and the physical examination. Two features in this connection deserve special emphasis: (*a*) The fact whether the organ involved is vital and (*b*) the possibility of relief from the inflammation either spontaneously or by surgical or by other procedures. For example, in Fig. 4, we have a blood picture which betokens a serious state when studied alone; but when one considers also the clinical facts that the abscesses did not invade vital organs and also that they could be and were efficiently treated (by drainage) we find a large part at least of the explanation of the patient's complete and fairly prompt recovery. (Study Fig. 5, too.) Here every feature of the blood picture is bad. The total leukocytes are low, indicating a poor resistance; the percentage of polymorphonuclears is high, demonstrating a severe infection; the index is very low and the total lymphocytes are down. The organ involved, a lung, is a vital one; and efficient treatment (by drainage or otherwise) was very difficult. If the part of the body invaded had been the appendix the patient probably would have recovered, other things being equal; for the appendix not being a vital organ (and being readily accessible) can be removed, and an appendicular abscess can be effectually drained. In Fig. 6, June 18, the blood picture looks very bad *per se;* but when one discovers that it is due to an abscess in the abdominal wall the picture takes on a lighter hue; for the wall of the abdomen is relatively not a vital portion of the body, and it is easy to treat curatively most abscesses which occur in this anatomic location.

7. **The Extent and the Form of the Leukocytic Blood Picture.** When making a blood examination we wish to emphasize the importance in all serious cases of including most if not all of the features described above. Without the total leukocyte count one is in the dark as to the amount of resistance the patient is offering. Without the percentage of polymorphonuclears one does not know the severity of the inflammation. Without Walker's index one is deprived of a lucid means of expressing the relationship between the total leukocytes and the percentage of polynuclears. Without the total lymphocyte estimation one misses valuable confirmatory evidence. A knowledge of the total number of polymorphonuclears per cubic millimeter is a distinct aid but is of the least value of any of the five features constituting our blood picture. The most important of all, without doubt, is the percentage of polymorphonuclears.

An examination of this sort may seem long and complicated to one who has not done several of them; but all that is involved beyond an everyday total and differential count is a few brief calculations and the printing of the blank charts. In our laboratory at present we are making the charts by hand; but later, when we feel we have digested the subject more thoroughly, we will have the printer stock us with a supply.

We wish to direct attention especially to the manner in which the data are charted. It is utterly impossible to convey adequate information to the mind through the eye by means of written characters collated in ordinary tables. We made tables for all of our cases, and of course obtained valuable knowledge from them; but the added information acquired when we transformed these plain tables into graphic charts was like a flood of light thrown into a poorly illuminated room. Charts with horizontal lines, one for each element of the picture (or constructed according to this principal) are very essential. This method gives perspective and throws into the foreground certain important features which otherwise remain unnoticed.

The Value of a Small Number of Leukocytic Counts. Very many writers emphasize the importance of making a considerable series of counts on any given patient in order to acquire information of appreciable use, and they deprecate the value of one count alone. We wish to emphasize the value of single counts. For example, in Case 6, Table 1, the surgeon relied completely on the blood picture from one examination to determine immediate operation. In nearly every case charted in this table the high percentage of polymorphonuclears, the negative Walker's index, the relatively small number of lymphocytes and the relatively large total count obtained from single examinations constituted exceedingly valuable exidence, and the story which these findings told was almost invariably confirmed clinically. On the other hand, low percent-

ages of polymorphonuclears and positive indices of resistance helped greatly to confirm the clinical diagnosis of mild and non-purulent lesions. Nearly all of these blood features were confirmed by operation or otherwise.

Conclusions. 1. That the details of the total white count considered alone have but little value as a prognostic index is evinced by the fact that segments of the curve may rise or fall or remain stationary while the patient's true condition is becoming either better or worse or is unchanged. However, the *general trend* of a curve composed of several counts, disregarding minor ups and downs, usually does have significance: a general downward course, other things being equal, parallels clinical improvement; an upward direction is of ill omen, and a horizontal course indicates but little change. We wish to emphasize most of all the fact that the total leukocyte count is a measure of the amount of resistance the patient is offering against the inflammatory process.

2. The count of the total polymorphonuclears runs somewhat parallel with that of the total leukocytes. However, this parallelism is not complete. We have made the discovery that these lines approach closest to each other when the patient's condition is the worst, and are farthest apart when he has returned to normal. Thus the convergence and the divergence of these two lines constitute a very good prognostic index to the course of an inflammatory disease.

3. The percentage of polymorphonuclears constitute a very reliable indication of the severity of an inflammation. A high percentage means a severe process almost without fail, and a low figure means a mild infection; but probably the low count cannot be relied upon to demonstrate absence of infection and especially of pus to the extent that a high count can be trusted to indicate a severe infection—usually with pus or gangrene or both.

4. The polymorphonuclear (Walker's) index of resistance is an exceedingly reliable prognostic guide. However, readings near normal (zero) must be interpreted in connection with the other features of the blood picture, especially the percentage of polymorphonuclears. If these are high the condition is serious or at least may become so, while if the polymorphonuclears are within the normal limit there is but little cause for apprehension. A very low index means by itself a serious condition, for the index cannot drop far unless the percentage of polymorphonuclears (measuring the severity of the inflammation) rises high or relatively high and unless at the same time the total leukocytes (indicating body resistance) register low or relatively so.

5. The total number of lymphocytes per cubic millimeter constitutes a very reliable index of a patient's state of resistance. A reading near or especially below lowest normal (1000) is unfavorable. The auspicious cases remain well above this danger

line. We have made the original discovery that the curve of the total lymphocytes parallels Walker's index (in the class of cases investigated), and also it seems to have practically the same significance as Walker's index; but like the latter it must be interpreted in connection with the percentage of polymorphonuclears and the total leukocyte count.

6. A hematologic picture has its true significance only when interpreted in connection with the clinical findings. While many of these are important, we wish to emphasize two: (1) the fact whether the part of the body concerned is vital, and (2) the possibility of relief, either spontaneously or by surgical or other means.

7. We consider that none of the features of the hematologic picture we have presented should be omitted in examining serious cases. However, if one must choose, there is no reasonable doubt that the total number of polymorphonuclears per cubic millimeter is the least important element and that the *percentage* of these same cells is the most important.

8. We desire to emphasize the value of a single blood examination, although, of course, we always prefer to get two or more counts, if possible, on any given case.

9. Negative findings have much value but are not to be relied upon as implicitly as positive ones.

10. We wish to emphasize the importance of depicting blood pictures in the form of graphic charts as described in this article, and we maintain that tables with written characters only, which omit the all expressive systems of lines, are very inadequate.

We regret that space will not permit the publication of our bibliography of about two hundred references.

TABLE I. This is made up to show the *value* of *single counts* in cases in which more than one enumeration was made. From two to twelve counts were made on each of these patients. One count from each case, in nearly every instance the one immediately preceding operation, was selected for this table. In Case 8 there was no visible discharge except the menstrual flow. The exact nature of the lesion never was ascertained because the patient did not come to operation. The count in Case 1 was immediately postoperative, which almost always is higher than a preoperative one. In case 47 the count was taken four days after operation—after the patient had improved greatly.

This table illustrates, among other features, the futility of attempting to diagnose with certainty the presence of pus by the percentage of polymorphonuclears or by the total count. Pus was present in percentages ranging from 64 to 94, and in total counts from 7,200 to 28,300. Pus was absent in percentages varying from 64 to 93, and in totals from 8,000 to 28,400. These findings are explained by the fact that there may be but little pus in a virulent infection and much pus in a mild one.

TABLE I.

Case.	Per cent polymorphonuclears.		Total leukocytes.		Diagnosis, etc.
	Pus or gangrene.	No pus.	Pus or gangrene.	No pus.	
38	77	..	6,500	.....	Abscess of kidney.
14	81	..	14,200	.....	Infection, puerperal; no operation.
21	..	75	.....	11,500	Appendicitis, acute; burn of foot.
8	..	93 (?)	.....	23,500	Infection, acute pelvic; acute gastritis; no operation.
4	81	..	16,000	.....	Abscess of retroperitoneal sarcoma.
1	..	84	.....	28,400	Eclampsia; Cesarean section.
3	..	66	.....	8,900	Appendicitis, acute catarrhal.
2	85	..	28,300	.....	Appendicitis, acute, purulent, gangrenous.
16	86	..	15,400	.....	Appendicitis, acute, purulent, gangrenous.
46	82	..	22,000	.....	Appendicitis, acute purulent.
47	69	..	12,000	.....	Empyema, postpneumonic. Patient two years old.
32	70	..	7,200	.....	Thrombophlebitis, puerperal, pelvic.
13	..	93	.....	28,200	Cyst of spleen; no gross signs of infection.
	84	..	15,000	.....	Infection, secondary, of laparotomy wound.
7	90	..	25,000	.....	Pneumonia, acute lobar; no operation.
31	91	..	13,000	.....	Abscess, pelvic; following radium treatment uterus; three operations.
11	89	..	10,000	.....	Abscess of lung; following traumatic infection of arm.
24	91	..	17,200	.....	Appendicitis, acute, purulent, gangrenous.
5	64	..	7,400	.....	Appendicitis, acute purulent.
17	..	64	.....	8,000	Appendicitis, subacute.
48	87	..	27,000	.....	Infection and gangrene, acute, of ovarian cyst (twisted pedicle).
	94	..	16,000	.....	Infection, secondary, laparotomy wound.

BURN OF FOOT—ACUTE NON-PURULENT APPENDICITIS

FIG. 1.—Case 21. Burn on the foot; acute appendicitis. Patient of Dr. S. L. Ledbetter, Jr. Mr. W. O. M. Age twenty-eight years. In hospital, September 25 to October 18, 1920. Patient entered hospital with a burn on the foot. After several days pain in chest developed accompanied by nausea and vomiting. There was no particular tenderness in the abdomen at first. Later, there appeared distinct localizing symptoms in the region of the appendix.

Operation and Pathology. Laparotomy by Dr. Ledbetter, October 5, 1920. No drainage. Appendix was large, red and swollen, but there was no macroscopic pus.

Postoperative Course. This was practically uneventful. Patient felt bad October 1; better on October 2; better on the 3d; about the same, on the 4th; not so well on the 5th. Temperature and pulse remained practically normal throughout convalescence. He was up in a chair October 13, and went home on the 18th.

TABLE II.

Case.	Total leukocytes.		Per cent polys.		Walker's index.		Total lymphocytes.		Diagnosis, etc.
	Pus or gangrene.	No pus.	Pus or gangrene.	No pus.	Pus or gangrene.	No pus.	Pus or gangrene.	No pus.	
6	18,800	.....	95.5	....	−16.7	.....	660	....	Appendicitis, acute; no macroscopic pus; gangrenous mucosa.
9	.....	12,200	....	64	.....	+8.2	....	3,900	Appendicitis, chronic; ulcer, gastric.
10	.....	8,200	....	71	.....	−2.8	....	1,930	Appendicitis, chronic.
12	.....	9,100	....	66	.....	+3.1	....	2,730	Salpingitis, chronic; retroflexion of uterus.
15	.....	6,000	....	65	.....	+1.0	....	1,260	Pyelitis, recurrent; salpingitis (?); no operation.
18	11,600	.....	84.0	....	−12.4	.....	1,220	....	Appendicitis, acute; pus abundant.
19	8,000	.....	56.5	....	+11.5	.....	3,120	....	Appendicitis, acute; amount of pus very small.
20	.....	6,800	....	59	.....	+7.8	....	2,210	Appendicitis, chronic; cystic ovary.
22	.....	9,500	....	57	.....	+12.5	....	3,090	Appendicitis, chronic.
23	14,300	.....	92.5	....	−18.2	.....	715	....	Cholecystitis, subacute; pus (?)
25	24,900	.....	83.5	....	+1.4	.....	3,490	....	Appendicitis, acute; gangrene; abundant pus.
27	.....	13,600	....	85	.....	−11.4	....	1,630	Nephroptosis; no operation; pus (?)
28	15,300	.....	87.5	....	−12.2	....	1,610	....	Appendicitis, acute; large amount of pus.
29	30,100	.....	95.0	....	−4.9	.....	1,050	....	Appendicitis, acute; gangrene; much pus.
30	27,300	.....	92.5	....	−5.2	.....	1,230	....	Appendicitis, acute; gangrene; much pus.
33	.....	8,300	....	56	.....	+12.3	....	3,200	Undiagnosed; no symptoms of acute infection; no operation.
34	.....	6,000	....	70	.....	+4.0	....	1,560	Obstruction of intestine, incomplete; no operation.
35	10,400	.....	65.0	....	+5.4	.....	3,220	....	Abscess of teeth, chronic; very little pus; teeth extracted.
36	.....	6,200	....	57	.....	+9.2	....	2,390	Appendicitis, chronic.
37	24,400	.....	85.0	....	−0.6	.....	2,810	....	Appendicitis, acute; gangrene; much pus.
39	.....	10,200	....	70	.....	+0.2	....	2,350	Colitis, mucous; no operation.
40	.....	6,200	....	65	.....	+1.2	....	1,740	Pyelonephritis; symptoms not acute; no operation.
41	.....	10,300	....	60	.....	+10.3	....	3,910	Hemorrhage, mild cerebral; no operation.
43	.....	15,200	....	74	.....	+1.2	....	2,900	Myocarditis and endocarditis, subacute; appendicitis (?); no operation.
44	.....	8,000	....	65	.....	+3.0	....	2,560	Lumbago, posttyphoid; no operation.
45	.....	10,400	....	63	.....	+7.4	....	3,330	Hemorrhage, uterine; cervicitis, chronic; retrodisplacement of uterus.
Averages	18,500	9,100	83.7	65.4	−5.2	+5.1	1,910	2,540	
Ranges	8,000 to 30,000	6,200 to 15,200	56.5 to 95.5	57 to 85	−18.2 to −11.5	−11.4 to −12.5	660 to 3,490	1,260 to 3,910	

TABLE II.—This is made up from patients on whom *single counts only* were taken. All were operated upou unless otherwise stated. Under total leukocytes note that while the average count is much higher in the purulent than in the non-purulent cases, yet it is possible to have pus with rather low counts, for example, 8,000 and 10,000 (Cases 19 and 35). In these instances, however, the amount of pus was so small as to be almost negligible. When any considerable amount develops the counts run from 12,000

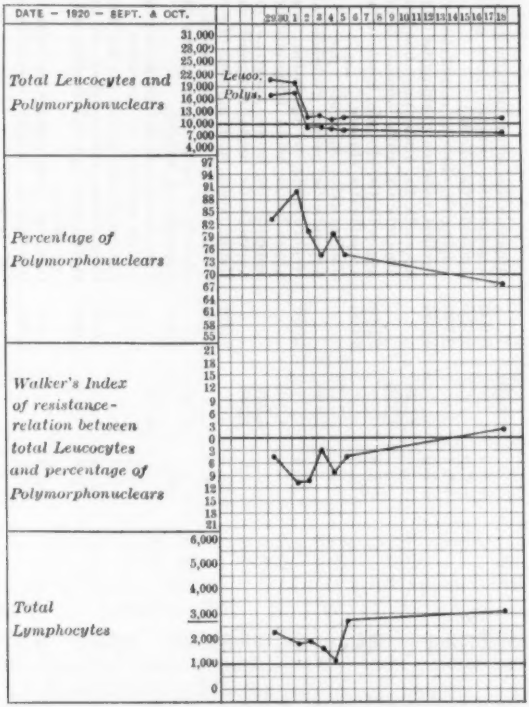


FIG. 1.—See general explanation, p. 555, and description in text.

to 30,000. And still with a high count there may be little or no pus (Case 6). In the non-purulent cases none of the counts are high, the largest being 15,200 (Case 43). Note that the range is 100 per cent greater with the purulent lesions.

In regard to the percentage of polymorphonuclears a low figure does not exclude pus, but the amount is apt to be small, for example, 56.5 per cent and 65 per cent in Cases 19 and 35. Percentages ranging from just above 80 to 95 show marked virulence and at the same time considerable pus usually, but not always; for,

observe that Case 6 with a percentage of 95.5 exhibited no macroscopic pus. The range of variation is greater by 30 per cent in the purulent than in the non-purulent cases.

Walker's index is usually minus in the pus cases and plus in the clean or relatively clean ones. Notice that the pus column has only three plus indices, two of which scarcely belong here because of the very small amount of purulent exudate. In the no-pus series there are only two minus indices. The purulent cases average minus 5.2 and the non-purulent ones plus 5.1.

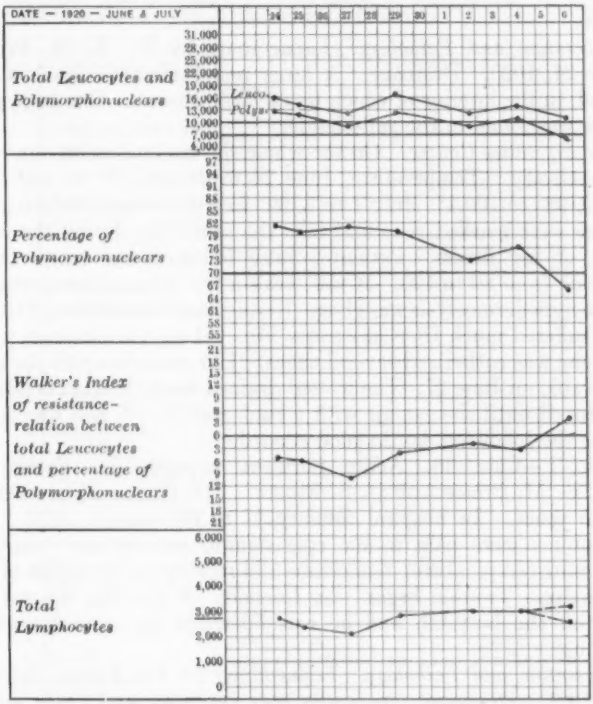


FIG. 2.—The count July 6 showed an erratic rise of the endothelial leukocytes to 8 per cent; this increase occurred at the expense of the lymphocytes. By counting the excess of endothelials in with the lymphocytes a slight increase in the total lymphocytes is produced as indicated by the dotted line. For further elucidation, see general explanation, p. 555, and description in text.

The total lymphocytes average lower by about 30 per cent in the purulent than in the non-purulent conditions. Also the range is somewhat greater in the former than in the latter. And still more significant are the low levels, well below 1000, to which the purulent cases now and then drop (Cases 6 and 23). This almost never occurs with the non-purulent lesions.

FIG. 2.—Case 4. Abscess of retroperitoneal sarcoma. Patient of Drs. E. M. Prince and D. S. Moore. Mrs. S. J. A. Aged forty-five years. In hospital June 24 to July 8, 1920. She had been in the hospital for a few days prior to the middle of June, 1920, with a history of gall-stone colic, and a diagnosis of cholelithiasis was made at that time. No other symptoms were present, and she was discharged without operation.

She returned June 24, 1920, suffering with acute pain, which had begun five days previously and which extended over her entire abdomen. Preoperative diagnosis of appendicular abscess was made.

Operation and Pathology. Laparotomy by Dr. E. M. Prince, June 24, 1920. Drainage. A large retroperitoneal sarcoma was found, in the interior of which was a large abscess. One large gall-stone was found in the gall-bladder.

Postoperative Course. On the whole she made a rather uneventful recovery. Temperature, June 24 to 28 was 97° to 102°; 29 to 30, 98° to 100.4°; July 1 to 3, 99° to 101°; 4 to 8, 98° to 100°. There were marked rises and falls the same day during the early part of her illness. Patient's pulse followed her temperature, ranging from 80 to 120. It was weak a few hours after operation, when hypodermoclysis was given. Respirations varied from 20 to 30. She suffered much from gas pains, etc. Many enemas were given and she was catherized several times. Her condition was the least favorable on June 27. The wound drained freely and her condition improved until she sat up with a back-rest July 7, and was taken home the following day in good condition.

FIG. 3.—Case 46. Acute purulent appendicitis. Patient of Drs. E. M. Prince and D. S. Moore. Mr. R. S. Aged twenty-seven years. In hospital January 17 to February 6, 1920. His symptoms were pain in the epigastrium, nausea and vomiting; moderate temperature; tenderness and rigidity in the region of the appendix. Trouble began the forenoon of the day the patient entered the hospital, and he was operated the same day about 8.00 P.M.

Operation and Pathology. Laparotomy by Dr. Prince, January 17, 1921. Drainage. Appendix was ruptured and there was a moderate amount of pus. No adhesions had formed.

Postoperative Course. Recovery was very satisfactory. Wound drained freely and there was still a little discharge when the patient left the hospital. Temperature at the time of operation was 102.68; this had fallen to normal by the nineteenth, and there was no subsequent rise. Pulse corresponded to temperature. He was on a back-rest the third and walked the sixth.

FIG. 4.—Case 31. Pelvic abscess; secondary in right iliac region; tertiary in left iliocostal space. Patient of Drs. E. M. Prince and D. S. Moore. Mrs. W. H. Aged forty years. In

hospital November 10, 1920, to January 16, 1921. Patient had received two treatments of radium for uterine hemorrhage, the last exposure being made a few days prior to her entrance to the hospital. After her first treatment her bleeding was lessened and after the second it stopped altogether; but a dark, malodorous vaginal discharge of moderate quantity appeared. During the twenty-four hours before she came into the hospital she had three chills and her temperature rose as high as 104°. She was observed for ten days in the hospital, when finally induration in addition to tenderness developed in the hypogastrium.

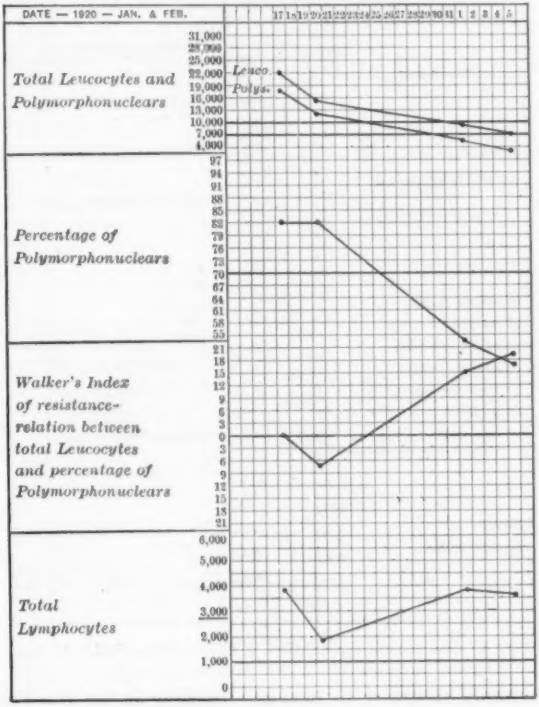

DATE — 1920 — JAN. & FEB.
Total Leucocytes and Polymorphonuclears
Leuco.
Poly.
Percentage of Polymorphonuclears
Walker's Index of resistance-relation between total Leucocytes and percentage of Polymorphonuclears
Total Lymphocytes

FIG. 3.—See general explanation, p. 555, and description in text.

Operations and Pathology. Laparotomy by Dr. D. S. Moore, November 20, 1920. Median incision above symphysis pubis. Drainage. A large amount of yellow, foul-smelling pus was evacuated; its origin was not ascertained.

November 27. Drainage incision in right inguinal region by Dr. Moore. A considerable, thick, rather malodorous pus was obtained; its source was not ascertained.

December 5. Drainage incision in left iliocostal space by Dr. E. M. Prince. A large amount of thick greenish-yellow pus escaped; its ultimate source was not discovered.

Postoperative Course. After the first operation the temperature ranged mostly from 100° to 103°; pulse, 85 to 105; respirations, about 20. After the second operation there was but little apparent change. Following the third incision the temperature, pulse,

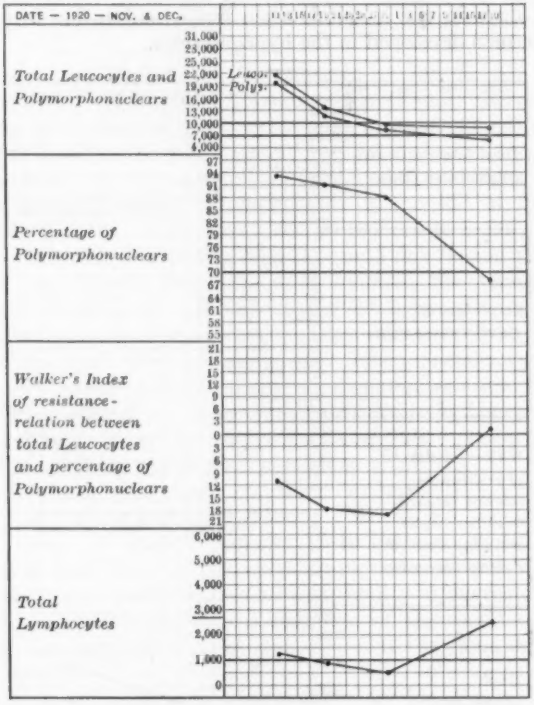


FIG. 4.—See general explanation, p. 555, and description in text.

etc., gradually returned to normal, reaching it for the first time permanently about December 30, although by December 18, there was marked improvement. All drainage had ceased by January 14, 1921, and January 16 the patient was discharged cured.

TRAUMATIC INFECTION IN RIGHT ARM; METASTATIC ABSCESSES IN LUNGS.

FIG. 5.—Case 11. Traumatic infection in right arm; metastatic abscesses in lungs. Patient of Drs. E. M. Prince, D. S. Moore

and C. Lull. Mr. W. J. J. Aged thirty-two years. In hospital September 10 to 28, 1920. Discharged from army on account of beginning locomotor ataxia. About six weeks prior to entering hospital he acquired a traumatic infection of the soft parts of the right arm near the elbow. About the time he entered the hospital signs of a metastatic abscess in the upper lobe of the right lung began to be evident. On September 22, roentgen-ray plates confirmed this diagnosis and showed also an abscess in the left lower lobe.

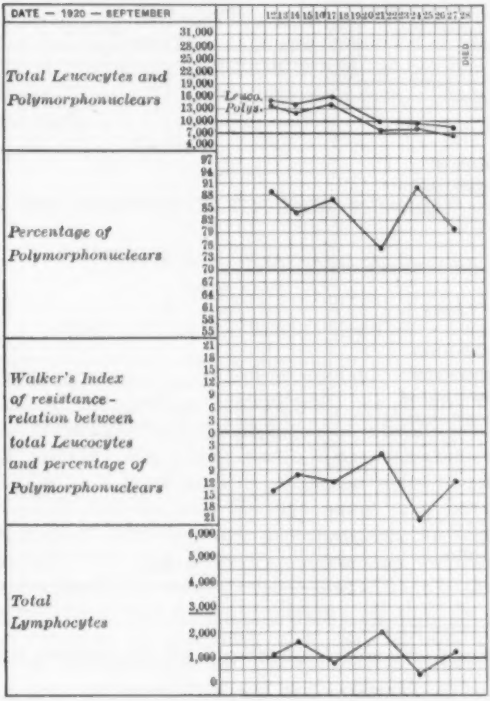


FIG. 5.—See general explanation, p. 555, and description in text.

Operation and Pathology. Incision and drainage of abscess in right lung by Dr. D. S. Moore, November 23, 1920. A large amount of pus was found.

Postoperative Course. Temperature rose and fell almost daily from about 99° to 104° throughout his illness while in the hospital. Pulse varied with the temperature, ranging from 110 to 140. Respirations were mostly from 20 to 25. There was no improvement after the drainage operation, November 23. He was expected to die November 24, but did not expire until November 28.

FIG. 6.—Case 48. Pregnancy complicated by infected, gangrenous ovarian cyst. Patient of Dr. Edward O'Connell. Mrs. A. McD. Aged twenty-nine years. In St. Vincent's hospital June 12 to 27, 1920. Married nine months. Prior to marriage, menstruation was irregular. Has had no abortions. Patient is about five months pregnant.

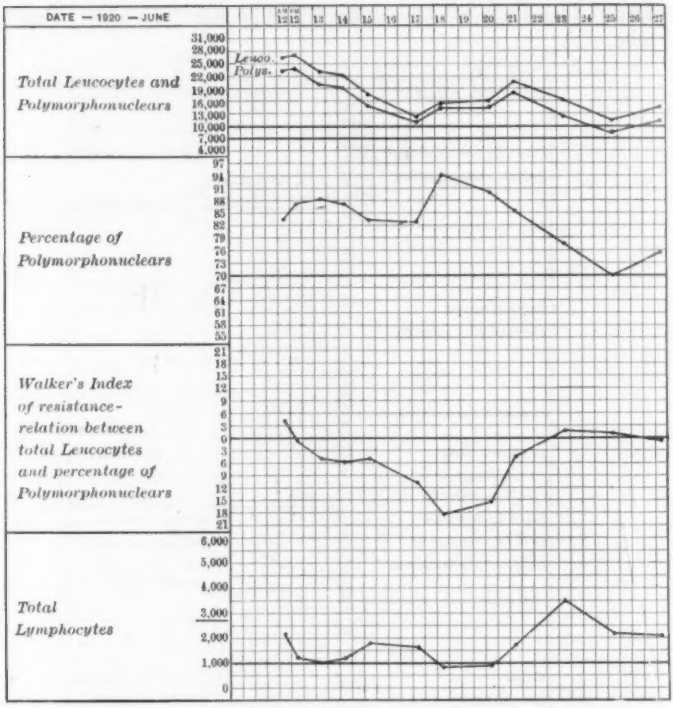


FIG. 6.—See general explanation, p. 555, and description in text.

About three months ago she began to complain of severe pain in the left side of the abdomen at intervals of about four days; this pain lasted four or five hours in each attack. Pulse and temperature were normal during intervals between attacks. She has been constipated and has suffered from headaches for about two months.

Operation and Pathology. Laparotomy by Dr. Watkins, January 13, 1921. Drainage. An ovarian cyst, about 18 cm. in diameter, was found, lying on the left side of the lower abdomen. The side of the cyst against the abdominal wall showed signs of moderate

inflammation. The pedicle was twisted and there was considerable beginning gangrene on the side toward the median line.

Postoperative Course. Temperature ranged from 96.2° to 100,° reaching the latter figure only once, namely, the day after operation. Pulse before operation was 108 to 110; the rest of the time it ranged from 78 to above 90, reaching 100 only January 19 and 20. Quality was practically normal all of the time. Respirations were 18 to 22, except during the two days before and three days after operation, when they ranged from 22 to 28.

There was some purulent discharge from the wound, especially January 18 to 20; on this latter day a large abscess was evacuated through the drainage opening. General condition of the patient was very good throughout the entire course of her trouble, and she went home January 27 in excellent condition. The pregnancy was not interrupted.

THE SURGERY OF THORACIC TUMORS.*

By Abraham O. Wilensky, M.D.
NEW YORK.

(From the Mount Sinai Hospital, New York.)

Intrathoracic surgery is still a pioneer field. We are fortunate in that much of the necessary groundwork has already been done in the physiologic aspects of the problems of intrathoracic surgery. The recent military emergency was a most valuable experience in that it gave to a large number of men a sense of security in operating within the thorax. So that many men have learned (1) the methods of incision which give maximum visibility within the thorax; (2) that the thoracic viscera may be manipulated without undue shock and without serious disturbance to the patient; (3) to control hemorrhage from the viscera; (4) that the lung may be cut and sutured and that parts of it may be removed safely; and (5) that intratracheal, intrapharyngeal or other forms of differential pressure anesthesia are not essential, although they are helpful and advisable when operating within the thorax. All of this experience is of the utmost value for the surgical problems of civil life.

More than anywhere else in the body the successful surgery of thoracic tumors has imperative need for early diagnosis. Then the lesion will be exposed when it is in its simplest and most uncomplicated state; when it is as small as possible, when its removal is not hampered by adhesions to vital structures or made impossible

* Read at a Symposium on Thoracic Tumors before the Yorkville Medical Society October 17, 1921.

or futile by reason of neighboring or distant metastases; and when the removal of the growth is not made dangerous by reason of secondary infection. Clinicians must constantly keep in mind that many of the so-called inflammatory lung conditions arising in middle or late life are, primarily, tumors and that the symptoms are called forth by superadded infection. I have no doubt that many of these are never discovered and go unrecognized with such generic diagnosis as pneumonia, bronchitis, bronchiectasis or pleural effusion of simple or tuberculous origin. It is of great importance in every case to make use of every available aid in diagnosis. Medical men must learn to submit their patients to the surgeon at an early period of the disease and all men, medical and surgical, must recognize the increasing necessity for exploratory intrathoracic operations if the maximum amount of good is to be ultimately obtained. Thoracotomy for this purpose is a comparatively harmless procedure when done under proper conditions and with proper precautions. Many cases are now seen much too late for the possibility of doing anything of a radical nature because medical men have hitherto been too timid about referring patients with obscure intrathoracic conditions for surgical exploration. It needs to be emphasized again and again how important it is for the medical men, and especially for the general practitioner, to learn the lesson that, when obscure intrathoracic conditions do not clear up fairly promptly under conservative forms of treatment, the chest be opened and adequately explored; under such conditions a wider margin of operability will gradually be obtained and, surely, many more lives be spared for an increasing number of useful years. Certainly unless this helpful attitude is exhibited by the medical men progress will never be made.

The use of the intratracheal and intrapharyngeal forms of anesthesia has been a great stimulus to the development of intrathoracic surgery. The method is especially useful and must be employed whenever there is expectation that both pleural cavities will be opened during the operative manipulations. There is danger of the latter happening as an accident in certain localities even when one is apparently operating in one pleural cavity only. Ordinarily, however, in operations in which only one pleural cavity is opened, the method is not essential and operations can be done with the ordinary forms of anesthesia. Nevertheless the use of the new methods is, decidedly, both a convenience and an advantage and, with their use, the patients do not appear to show to such a large extent the effects of shock or of an acute pneumothorax. When skilfully administered the movements of the lobes of the lungs during respiration are quiet and not excessive and the operator is not hampered in his manipulations. The method has an additional usefulness at the close of the operation when the wound in the chest

wall is to be sutured; the lungs are distended so that they entirely fill the chest and lie in close approximation to their corresponding parietal pleural surfaces, the object being to obviate any dead space, *i. e.*, any pneumothorax, within the pleural cavity.

Access to the interior of the chest can be obtained in a number of ways. In general these conform themselves to one of three types: (1) In the first, an opening is made, as in the usual thoracotomy, by resecting one of the ribs; with this incision visibility is bad and manipulations are difficult. (2) In the second a trapdoor is cut in the chest wall by division of the ribs and soft parts; when this is turned out, one side of the flap acting as a hinge, a fairly large opening can be obtained. Visibility is, however, only fair through such a window and access to the organs is only moderately fair except in certain favorable locations. (3) In the third, a long intercostal incision is made in the sixth or seventh interspace and the ribs are forcibly separated by a powerful retractor; additional room is obtained by dividing one or more ribs at the posterior extremity of the incision near their angles. This is the best universal incision; it gives the maximum visibility and access to all the organs within the chest; and manipulations are most easy to execute. When sutured no deformity is apparent. For work on the lungs and diaphragm, or for intrathoracic esophageal operations the incision is not surpassed by any other for access and exposure. The degree of shock seen after operations done through such an incision is at a minimum.

The immediate dangers of intrathoracic operations include the following:

1. **Acute Pneumothorax.** This complication is entirely preventable by the use of the intratracheal, intrapharyngeal or differential pressure forms of anesthesia. In operations involving only one pleural cavity and done without this latter aid the acute pneumothorax is only exceptionally provocative of sufficient embarrassment to excite concern. One usually sees a moderate increase in the number of respirations; more or less cyanosis; and some irregularity of the cardiac action. The embarrassment is only shortlived and very quickly the effects of the pneumothorax are so negligible as to be hardly distinguishable in the clinical picture. In exceptional cases pneumothorax is accompanied with marked disturbances of respiration and circulation which rapidly lead to collapse of the patient and frequently to a fatal termination. I repeat for emphasis that in operations involving both pleural cavities such severe and dangerous forms of acute pneumothorax are only prevented by the use of the new forms of anesthesia.

2. **Mediastinal Flutter.** In normal respiration the integrity of position and action of the central mediastinal portion of the intrathoracic contents is maintained by similar normal conditions in

the adjacent lateral cavities of the chest. If the static conditions on one side are suddenly disturbed by an operatively produced open pneumothorax the entire mediastinal structure is caused to assume a lateral motion because of the passage of air into and out from the open chest wound unless provision has previously existed, or has been introduced during the operation, which is capable of preventing this lateral mobility and of holding the mediastinum immobile in a relatively normal position. This is a very serious phenomenon: It can quickly disturb the normal functions of the heart and of the large vessels and cause marked embarrassment of the pulmonary and general circulation sufficient to bring the patient into a state of collapse from which recovery is rarely possible. The important lesson to be remembered in operating within the thorax, especially upon the lungs, is that the mediastinum be steadied by traction upon the root of the lung, or upon the stumps of the lobes after lobectomy.

The combination of an acute pneumothorax with mediastinal flutter is perhaps accountable for the most severe of these clinical pictures.

3. **Hemorrhage and Shock.** With ordinary care hemorrhage, both intrapulmonary and intrapleural, should be entirely preventable. Shock is an important factor and is aided and abetted by acute pneumothorax or mediastinal flutter, or by both of the latter together.

4. **Opening of the Pericardium when Operating on the Left Side is a Serious Complication.**

The late dangers of intrathoracic operations include the following:

1. *Pleurisy.* Pleuritic effusions commonly appear after operation. This does not seem to be preventable at present and is frequently of a purely mechanical origin. When uninfected they are not dangerous; and when they do not disappear spontaneously they can be withdrawn.

2. *Pneumonia.* Pneumonias are common even when the center of operation is outside of the lung proper. One distinguishes two varieties, the least common of which is the lobar type; much more frequently forms of broncho- and lobular pneumonia are present. All of these are cause for anxiety until they are thoroughly resolved.

3. *Infarction of the Lung Occurs after Lobectomy.* This seems to have important relations to the number and size of the vessels which must necessarily be tied during the operation. Pneumonic infiltrations are naturally common on the borders of the infarctive areas. It is important to differentiate these lesions from intrapulmonary hemorrhages produced during the operative manipulations.

4. *The Great Danger of Operating Within the Thorax Lies in Infection.* Most of the late fatalities occur because of this cause. Infection may take place as a fulminating process, resulting rapidly in death, or, more commonly, more slowly. Infection may take place in the pleural cavity or within the mediastinal cellular tissue. Usually the infection takes the form of an empyema; these can be severe and can result fatally, or they can be mild affairs which serve simply to prolong the healing and the convalescence. A very severe form is due to an anaërobic infection which arises in tumors that are breaking down, and which causes a gangrenous form of inflammation of the entire operative wound. The bad infections are those which take root in the mediastinal cellular tissue; practically invariably these result fatally. These infections are to be feared and guarded against in any operation in which the mediastinum must be opened; in esophageal operations it is the commonest cause of failure. The process has no distinctive clinical signs and is assumed to be present whenever the signs of sepsis appear after any operation in which the mediastinal cellular tissue is exposed. There is no satisfactory method of drainage which can prevent the spread of the infection and death usually ensues with the clinical picture of a high grade of sepsis.

5. Persistent sinuses are fairly frequent after operations on the lungs and are most principally due to bronchial fistulæ. Fistulæ almost always appear after lobectomy but, luckily, most of these close spontaneously.

The question of *drainage* after intrathoracic operations is most important. As a general rule it is to be avoided as much as possible. Its omission is conducive to more comfort in the postoperative period and it permits a better static condition within the thorax for the carrying on of the functions of circulation and respiration. Unfortunately, however, there are many contingencies which demand the insertion of drainage and in such eventualities the drainage should be provided with these purposes in view.

The operability of thoracic tumors and the risks entailed in operation are determined upon general and local grounds; the latter hold similarities to those of tumors in other regions of the body. I shall discuss them with the individual varieties of tumors encountered. Because operations within the thorax are necessarily extensive and productive of much shock, it is necessary to choose one's patients carefully; old decrepit patients or those with advanced circulatory or pulmonary disease are not fit subjects for intrathoracic operations. Even in those who are robust one must be prepared on occasion to fortify the dangerous intervals by the use of transfusions of blood. The total surgical experience in regard to these aspects of intrathoracic surgery is still rather limited by the comparatively small number of cases on record; with more extensive experience our knowledge in regard to these matters must be considerably broadened.

Chest-wall Tumors. In actual practice about 72 per cent of chest wall tumors are malignant (carcinoma, sarcoma and hypernephroma); about 20 per cent are benign and of these the common types are fibroma and chondroma; 2 per cent are exostoses or are due to syphilis. About 28 per cent begin in the ribs and about 21 per cent in the sternum. An important group belong to the carcinomata of the breast which spread into the chest wall. Eighty-five per cent of the tumors are found from the second to the seventh decades of life. The influence of trauma seems more marked with these than with tumors arising in other regions of the body. The differential diagnosis must be made between tumor, cold abscess, syphilis, exostosis, aneurysm or dermoid cyst.

With tumors of such accessibility it would seem that the roentgen rays or radium would be very efficient therapeutic agents, but unfortunately this is not so in actual practice, and although isolated cases have been reported by Turner and others, as a general rule these agents are of not sufficient permanent benefit to warrant giving them the place of first choice. Surgery still holds first place and is still the best therapeutic means. A radical operation is possible in about 20 per cent, a palliative excision is permissible in another 25 per cent and the remaining 50 per cent of the cases are hoplessly inoperable. The main contraindications to radical operation are the presence of metastases, or the size of the growth and the extent of involvement of neighboring and contiguous structures. In considering the presence of metastases it is important to remember that not all shadows which are visible roentgenologically in the chest cavity are tumors; and, secondly, in excluding metastatic foci in the bones the Bence-Jones test is very valuable.

The operative technic is not exceptionally difficult. A block excision of the tumor-bearing portion of the chest wall is done by division of the ribs and soft parts; the extirpation naturally requires a sudden acute pneumothorax and collapse of the lung. In the lower ribs the diaphragm must be cut into so that frequently there results a combined thoracolaparotomy. Intratracheal or intrapharyngeal anesthesia is especially useful in chest-wall tumor extirpations. At the conclusion of the operation it is of great importance to be able to distend the lung completely and suture it to the margins of the resultant chest-wall opening. The latter is closed by a plastic of the adjoining skin and soft parts. In certain locations—the anterior thoracic wall—the opposite breast can be mobilized and displaced across to the operated side to obturate the opening; this technic is especially useful with carcinoma of the breast involving the chest wall. When no other technic is available the opening is plugged with gauze. Operations done in more than one stage may be helpful.

The mortality of operation is about 13 per cent. The chief

causes of death are shock (33 per cent), pneumonia (25 per cent) and empyema (25 per cent). Chest-wall tumors show a great predisposition to postoperative infections.

The amount of resultant deformity varies, depending on the number of ribs and the area of chest wall which is resected; but even following wide excisions there seem to be no untoward effects from the absence of ribs and soft parts. In several patients about whom I know, there has been no disability as far as their daily work is concerned.

Recurrences are fairly frequent and multiple operations have been done when the tumors have recurred locally. Early radical extirpation offers the best prospect of cure; even in the presence of extensive involvement it offers the best prospect for a relatively long period of freedom from recurrence.

Pleural Tumors. The best classification of pleural tumors is that of Guyot and Parcellier and includes: (1) The benign tumors, including the usually found lipomas, chondromas and fibromas; (2) mixed tumors, such as chondrosarcomas, myxofibrosarcoma and myxoliposarcoma (Pallasse and Roubier); (3) the malignant tumors. Primary malignant tumors of the pleura are among the uncommon neoplasms and are limited to sarcoma (about 20 per cent) and endothelioma (about 80 per cent). There is a good deal of discussion in the literature in regard to the origin of the latter group of tumors; the controversy ranges between those who believe that these tumors originate in the lining cells of the pleura (Ribbert, etc.) and those who believe that they originate in the pleural lymphatics (Schultz and Eppinger).

Up to 1909 there were about 96 cases in the literature. Pleural tumors are found twice as frequently in men as in women and the greatest number are found in patients between forty and sixty years of age. It appears to be a little more common on the right side than on the left.

Pleural tumors are usually insidious in their origin and growth and patients appear for medical care at comparatively late periods when asthenia and cachexia are marked. A frequent picture under which the tumors masquerade is that of a pleural effusion. The differential diagnosis must be made from tuberculosis and tumor of the lung and bronchi. The roentgen ray is usually of little help; it should be done both before and after the fluid is withdrawn. Air or oxygen inflation may demonstrate a tumor which otherwise would be invisible. When effusions are present they may possess characteristic gross appearances; when not, positive information may in many instances be secured from a histological examination of the cellular content of the effusion after the sediment has been appropriately hardened and sectioned (Widal and Ravaut, Warthin, Warren, Mandlebaum).

As regards the therapeutic possibilities, pleural tumors are best

classified with tumors of the chest wall; surgery still holds first place. Guyot and Parcellier found an apparent operability in only 27 per cent of 29 cases. An exploratory thoracotomy is always justifiable in the hope that the anatomic conditions may permit a radical removal.

The late results are very bad; recurrences in the operated cases have always appeared. It is to be hoped that in the future much better results will follow the combined use of operation and radium or roentgen-ray therapy.

Lung Tumors. Malignant disease of the lungs forms about 2 per cent of all cancer cases. Statistics tend to show that its frequency is apparently on the increase, but the latter is undoubtedly due to the fact that its recognition is becoming more general among competent medical men. The secondary tumors are more common. Practically all the ordinary varieties of malignant tumor are found to metastasize in the chest—sarcoma, carcinoma, melanosarcoma, hypernephroma, chorionepithelioma, lymphosarcoma and endothelioma. The differentiation is made upon two essential facts: (1) The general and local signs of a lesion in the chest either in the lung or pleura; and (2) the history or demonstration of a primary growth. Chorionepithelioma is known to be able to disappear spontaneously; otherwise nothing of value is possible therapeutically.

The primary lung tumors are much less common. It is important to differentiate those that originate in the bronchi from those that originate in the lung parenchyma. Benign tumors are very infrequent and are usually found at autopsy. In the bronchi they include (1) adenomas which originate in the mucous glands of the submucosa; (2) lipoma and (3) papilloma which are very rare; (4) chondroma, which is usually solitary and may calcify; and (5) osteoma. In the lungs benign growths are curiosities.

The malignant tumors, both of the bronchi and lungs, are, however, much more common than is generally supposed. In the bronchi they include spindle- and round-cell sarcomas and carcinoma. In the lung parenchyma they include (1) carcinoma, which usually begins to grow either at the hilus or near the visceral surface; (2) sarcoma, which usually begins to grow near the hilus; and (3) endothelioma, which originates on the surface of the lung.

The symptomatology of lung tumors shows a general resemblance to that of other pulmonary lesions. One distinguishes a broad group of general symptoms such as those one finds with lesions in general and tumors in particular. As regards the focal signs these differ with the location and gross characteristics of the neoplasm. In the pleural type of growth the symptomatology is very similar to that of a pleuritis with or without an effusion. In the hilus type of tumor the symptoms are those of a chronic bronchitis, bronchiectasis or lung abscess; these neoplasms grow

more rapidly, produce pressure symptoms and form metastases. The symptoms include cough, with or without a profuse expectoration, pain in the side, fever, loss of weight and strength, and the others commonly seen with such diverse lesions as a tuberculosis produces.

Roentgenologically there are nodular and infiltrating types of growth. The former seems to be less common and consists of various sized and distinct masses in the parenchyma and near the roots. Sarcoma is especially apt to extend out along the septum between the upper and middle lobes. Primary carcinoma consists of an infiltrating mass near the root and extending out along the bronchial tree. The characteristics of secondary tumors are the following: Metastatic sarcoma consists of sharply outlined nodules occupying more particularly the parenchyma. Hypernephroma produces a general infiltration of small miliary bodies, sharply defined and extending out from the roots. Metastatic carcinoma occurs as (1) a nodular type of indefinitely outlined fuzzy masses located at the roots and in the parenchyma; (2) an infiltrating type, which is most common, and which begins as a thickening near the hilus and gradually shades off; and (3) a miliary type resembling miliary tuberculosis except that the areas are larger, more dense, and more sharply outlined (lymphangitis carcinomatosa).

The bronchoscope is an important aid in diagnosis. Yankauer has pointed out that 12 per cent of the cases which he has examined through the bronchoscope have had malignant disease. A definitive diagnosis is possible when a piece of tissue can be excised. Similarly positive diagnoses are possible in the cases with pleuritic effusions in which the sediment of the fluid contains tumor cells.

Much experimental work has been done in animals on the removal of one or more lobes of the lung (Sauerbruch, Johns Hopkins group, Rockefeller group). Lung extirpation in animals is technically a simple matter; it is far more difficult in humans. Experimental animals recuperate more quickly because they are not hampered by any preëxisting disease of long standing. Operations have been done successfully in man, although their number is very few.

Access to the interior of the chest is best obtained by the long intercostal incision previously described. As a general rule as soon as one has determined that no metastases are present and that the tumor is technically removable, the portion to be excised is delimited and is tied in sections with a number of chain ligatures; the tissue is divided with the knife or, better still, with the actual cautery. The handling of the bronchial stump is always a matter of difficulty and fistula formation is exceedingly common. For this reason a number of different technics have been devised, all of which aim to avoid this complication; but all of them are uniformly and equally unsuccessful in the same proportion of the

cases. The simplest method—that of securely tying the stump after crushing with a heavy clamp—is the equal of any. The fistula, when it occurs, is best allowed to close spontaneously and in the greatest number it so does. Under such technic a form of air-tight drainage is essential. Healing takes place by granulation and the bronchial stump becomes covered by a mass of scar tissue.

The lung has a rich lymphatic supply and the operability of cases of malignant tumor would naturally be chiefly determined by the situation and extent of the primary tumor and by the amount of metastatic formation nearby in the glands at the root of the lung, or in the lower triangle of the neck, or at distant locations. The latter are specially frequent in the brain, in the suprarenals and in the thyroid gland. The technical difficulties vary with the situation of the tumor: When the tumor is near the surface of the lung, excision is comparatively easy; when the growth is near the hilus the difficulties are many. At the root of the lung there is comparatively more difficulty in securing a complete hemostasis; the danger of postoperative hemorrhage is larger; there is more likelihood of pulmonary infarction. It is advisable and necessary that a sufficient length of main bronchus remain after the ablation of the lobe of the lung to permit a satisfactory closure. Hitherto when the stump of bronchus promised to be too short, it was thought that operation would be impossible; it is to be hoped that a technic will be developed in which operation willl be made feasible because of the use of fascia transplanted into the defect in the bronchus which results after the lobectomy. Extirpation of the lower lobes is less difficult technically and is less dangerous clinically than extirpation of the upper lobes.

There are still far too few human cases of radical operation for pulmonary tumor to enable one to formulate any accurate opinion as regards the ultimate possibilities; up to the present all have been fatal (Helferich, Heidenhain and Murphy, Garré, Kummel). Some idea of the possibilities can be perhaps gained by comparison with lobectomy for lung abscess; the best statistics (Lilienthal) available at present show that a successful issue can be expected in about 50 per cent of the cases. If such results are possible with the badly infected lung abscesses, surely much better results can be expected with the comparatively clean cases of lung tumor. In animals the results vary with the skill and experience of the individual worker: In some series the mortality is about 5 per cent; in others it reaches to 85 and 90 per cent. The cause of death in animals includes sepsis and leakage from the bronchial stump. Marked transudations of clear fluid into the pleural cavity occur in one-half of the cases.

When only one lobe is removed the remaining lobes of the lung quickly fill up the vacancy left by the extirpation. When an entire

lung, however, is removed a number of factors contribute toward the obliteration of the cavity. These include: (1) Expansion of the remaining lung with (2) the dislocation of the mediastinal structures toward the operated side; (3) flattening of contraction of the thoracic wall with its attendant scoliosis; and (4) the elevation of the diaphragm. The largest part is played by the heart and lungs. Commonly an enclosed pneumothorax results which in time is aborted coincidently with the obliteration of the cavity; in a few cases the pneumothorax persists for an extraordinary length of time. There is evidence to show that the heart undergoes some hypertrophy.

The removal of one or more lobes of the lung seems to have no effect upon the longevity of animals.

In recent years bronchoscopic technic has improved to such a degree that it has been found possible by Jackson in a particularly favorable case to remove an endothelioma of the bronchus endoscopically. It is to be hoped that the successfully treated cases of this nature will continually increase. One of the dangers, however, which must be remembered is that the bronchoscopic technic gives but a limited field of vision and the visible tumor removed may be a small part of a large growth. Another danger is that a serious and fatal hemorrhage may follow, if an endoscopic removal of a vascular tumor be attempted. Bronchoscopic excisions should only be attempted in the most favorable of conditions.

The bronchoscope permits one palliative procedure which is useful in tumors originating in the bronchi or near the roots of the lung. Commonly bronchiectatic dilatations occur; or the tumor, breaking down and becoming secondarily infected, gives rise to a lung abscess. In either case a most deplorable condition results: The suppurating process, because of its profuse expectoration and most offensive odor, causes the patient to become a nuisance both to himself and his immediate family. For these patients some amelioration is possible by intratracheal and intrabronchial washings through the bronchoscope (Yankauer).

Mediastinal Tumors. Primary tumors of the mediastinum are chiefly those originating in the lymph nodes and pathologically are usually the lymphogranulomatous type of tumor—Hodgkin's and lymphosarcoma. It is important to remember that in Hodgkin's disease involvement of the intrathoracic nodes occurs in 25 per cent of the cases. (Wessler). The chief roentgenological characteristics are (1) mediastinal tumor; (2) isolated nodules or tumors in the lungs; (3) infiltrative changes; and (4) discrete nodules at the roots of the lungs. The type most commonly found is type 3, almost always with one of the others.

Patients with far-advanced tumors of the mediastinum lead a wretched existence. Compression of the large vessels—the superior and inferior vena cava—and of important nerve trunks makes

their lives miserable. Owing to the fact that invariably the patient reaches the surgeon in a far-advanced stage of the illness the tumor is inoperable because of technical reasons. What would be possible if these patients were referred to the surgeon at an early and opportune moment still remains to be seen. At the present time all that can be done surgically is of a palliative nature and consists of providing additional room within the bony thoracic cage for the increase in growth of the tumor so that the extreme discomfort can be alleviated. These decompression operations serve a similar purpose to those practised on the skull for the relief of brain tumors. The technic has been developed by Friedrich and by Sauerbruch and consists essentially in dividing the bony chest wall (1) through the middle of the sternum either transversely or better longitudinally, or (2) directly alongside of it. In suitable cases the purpose can be achieved under local anesthesia.

In very late cases considerable dyspnea develops, which is due to compression either of the trachea low down near the bifurcation or of its main divisions near the latter. The marked accompanying cyanosis frequently raises the question of the propriety of doing a tracheotomy; but this is useless for the reason that the point of obstruction is much below the point of attack. The only method available is to intubate the trachea and to insert a rigid catheter below the obstructed area in the bronchus. Conditions are precarious then and death is usually not far removed.

The mediastinum is one of the points of election for the appearance of dermoids and teratomata; the former are cystic and the latter are solid types of growth. They spring from embryonic inclusions. Surgical interference has hitherto been advised only when these seriously interfere with the circulation or with respiration. An excision *in toto* has been successful in only one case. A conservative form of attack is to marsupialize the cyst.

Tumors of the Heart. Tumors of the heart are still autopsy findings and are medical curiosities more than anything else. In the present state of knowledge they are beyond the reach of any method of therapy except perhaps the roentgen ray and radium.

Roentgen-ray Treatment of Intrathoracic Tumors. The treatment of intrathoracic tumors by radioactive agents—the roentgen ray and radium—is still in an unsettled state. It seems that in order to administer these agents successfully very large doses are necessary both to avoid irritating the tumor into an increase of growth and to cause successfully the death of all of the tumor cells, including especially those situated most distantly. Rays of sufficiently deep penetration are absolutely necessary. The principal difficulties in the technic lie with the safe methods of administration whereby such relatively enormous doses can be exhibited without causing stubborn burns of the skin and necroses of various kinds in the neighboring deep organs. Such excessively large

amounts of radioactive energy directed at any animal body commonly result in an artificial severe anemia and severe collapse which demands the immediate recuperation of the patient by vigorous means including transfusions of blood. Fatalities have occurred. It takes nicety of judgment to gauge the dose of radioactive energy accurately consistent with producing the maximum results with the minimum of damage. Much better work in this regard had been done in the European centers than in this country. A great deal of intensive work is constantly going on which has for its immediate object the avoidance of these difficulties and dangers and the improvement of radioactive therapy.

Tumors of the lung of the types usually found do not lend themselves readily to any beneficent effect from treatment with the roentgen ray or radium. Much better results are obtained with the tumors originating in the lymph nodes. There seem to be better average results in lymphosarcoma than in Hodgkin's disease, but in both the tumors can be caused to shrink and to disappear. Unfortunately, however, these are usually only temporary phenomena and the tumors rapidly recur. Lewis had a case in which a mediastinal tumor recurred three times after the apparent disappearance which followed radioactive therapy; finally the tumor recurred for the fourth time and the condition ultimately proved fatal. In none of these types of tumor does the disappearance of the tumor coincide with any change in the blood findings. It is to be hoped that with continued experience much more knowledge will be obtained which will permit a more effective and lasting disappearance of these tumors.

Where the tumors are accessible, technically operable and can be safely removed with the knife, the latter method is still the preferable one. Otherwise the tumors should be attacked with the roentgen ray or with radium. In operated cases the latter should be employed as a subsidiary measure.

Esophageal Tumors. With esophageal tumors one is more fortunate. Owing to the comparative slowness of growth of the malignant tumors of the esophagus—practically always carcinoma—the diagnosis can still be made in most of the cases while the lesion is still confined to the esophagus.

The earliest attempts at esophageal operations made use of the dorsal approach through the posterior mediastinum. The later group of experiments dealt with the transthoracic approach. Experiments were carried out on the cadaver, on animals and in certain instances human operations were also in the nature of experiments. Up to within the last year the method of approach was universally the second.

In dealing with resection of the eosphagus it is necessary to remember that besides the excision of the tumor-bearing area provision must be made for the reëstablishment of the alimentary

canal. The mobilization of the tube for the length necessary for suture in any portion of the esophagus proper is not possible beyond a distance of perhaps one inch. At the cardiac end of the esophagus the adjacent end of the stomach may be mobilized for a distance of not more than two inches. In either case even when the necessary mobilization is possible the suture line lacks the security present in intestinal suturing by reason of the absence of the peritoneum or of a similar protective structure; leakage almost invariably occurs. Another method must then be available to secure a successful result.

It has been found in actual practice that, owing to the fact that the upper segment leaks always and produces a fatal mediastinitis, it is necessary to remove the esophagus entirely from the chest. This is an extremely hazardous operation and up to the present has succeeded in only one case of Török. Unfortunately it has not been possible for Török or for any one else to repeat this primary success. In the last year Lilienthal has turned from the intrathoracic method of attack to the earlier approach via the dorsal mediastinum and has devised a technic which first seals off the mediastinum and prevents a mediastinitis; secondly, permits the excision of the tumor-bearing area; and, thirdly, permits a plastic operation for the restoration of the continuity of the canal. He, too, has had one successful case, but this again is an isolated instance and it remains to be seen whether this will be repeated by himself or by others before a final judgment is possible. America deserves great credit for having these two successful cases to its record.

The causes of failure with esophageal resections are chiefly shock and infection. The operability of the tumor is determined by the local characteristics of the growth, the presence of glandular metastases, the situation of the tumor, and the adhesions to important structures. A tumor which has perforated is absolutely inoperable because of the danger of infection in the mediastinum. Naturally there are not sufficient data available to enable an accurate judgment as to the actual proportion of operable cases, but it would seem fair to say from one's general experience that about 50 per cent of the cases of carcinoma of the esophagus are in an operable condition when they are first seen by the surgeon.

It is necessary to repeat again and again—even, perhaps, to the point of boredom—that the successful surgery of intrathoracic tumors requires the greatest coöperation on the part of the medical men. Early diagnosis is imperative and early surgical exploration is a *sine qua non* of success. Medical men, too, must bear with the surgeons in the difficulties and disappointments of their early attempts until a satisfactory technic is established which can cope safely with these newer and difficult problems.

REFERENCES.

1. Blumgarten: Am. Jour. Med. Sc., 1921, **192**, 377.
2. Carisi: Riforma Medica, 1920, **36**, 1124.
3. Du Bray and Masson: Arch. Int. Med., 1920, **26**, 715.
4. Eastwood and Martin: Lancet, 1921, **201**, 172.
5. Gack: Lancet, 1921, **200**, 1286.
6. Hedbloom: Arch. Surg., 1921, **3**, 56.
7. Heuer and Dunn: Johns Hopkins Hosp. Bull., 1920, No. 348, **31**.
8. Jackson: Tr. Am. Laryng. Assn., May, 1916.
9. Lemon and Doyle: Am. Jour. Med. Sc., October, 1921.
10. Lilienthal: Ann. Surg., 1921, **74**, 259.
11. Pallasse and Roubier: Ann. de Med., 1916, **3**, 243.
12. Pfahler: Am. Jour. Roentg., 1919, n. s., **6**, 575.
13. Warren: Arch. Int. Med., 1911, **8**, 648.
14. Warthin: Med. News, 1897, **71**, 489.
15. Wessler: Jour. Am. Med. Assn., 1920, **74**, 445.
16. Widal and Ravaut: Comp. rend. Soc. de Biol., 1900, **52**, 648.

THE DIAGNOSIS AND TREATMENT OF AMEBIC COLITIS.*

By Alfred C. Reed, M.D.,

ASSOCIATE CLINICAL PROFESSOR OF MEDICINE, STANFORD UNIVERSITY MEDICAL SCHOOL, SAN FRANCISCO, CAL.

Horace Greeley made a comment worthy of closest scrutiny by medical writers when he said, "I have not time to be brief." In discussing today so broad a subject as the diagnosis and treatment of amebic colitis, and a subject with so voluminous a literature, it would be improper to present other than a clear and condensed outline of the practical matters at issue. For that reason extended historic and literature references will be omitted, laboratory phases will not be discussed and attention will be centered on the practical clinical features of the subject.

Confusion has arisen from the indefinite use of the word dysentery. As employed here dysentery refers to a clinical syndrome of frequent bowel movements associated with pain, tenesmus, and mucus and blood in the dejecta. In this sense dysentery is purely symptomatic and not at all a disease entity in itself. A classification of its causes is easily made and helps materially in clinical study of the patient.

1. Dysenteries of bacterial origin.
2. Dysenteries associated with other definite diseases such as tuberculosis and syphilis.
3. Dysenteries due to toxic substances such as mercury and arsenic.

* Read before the annual meeting of the Utah State Medical Society, September 15, 1921, Salt Lake City, Utah.

4. Dysenteries due to irritants, as in the orient, chopped pig bristles and bamboo spicules.

5. Dysenteries due to animal parasites. In this group are the dysenteries of kala azar, pernicious malaria and trematode infections. Also are included ciliate and flagellate dysenteries which are of commoner occurrence than ordinarily estimated, and finally amebic dysentery.

Amebic infection is widespread in all hot climates of the earth and has been known in many sections of temperate climates. Due to its wide dissemination it has ceased to qualify as a strictly tropical disease in the last few years. In the United States it is becoming prevalent in all sections. Little is known of its endemic distribution at the present time. Factors which have dealt largely with its recent increase are (1) the return of soldiers after the World War, (2) increased streams of travel and heightened excursions of migratory labor and vagabonds, and (3) influx of foreign population elements into American agricultural and rural districts.

In England, H. A. Bayliss[1] states that amebic dysentery is common and estimates that 6 per cent of the adult males at home are carriers. As early as 1913, H. Z. Giffin,[2] in the middle northwest of the United States, reported 148 cases of Entameba coli and 79 cases of Entameba histolytica in 1700 persons examined. Reports and clinical experience of amebiasis increased until, in 1920, after examining 2300 returned overseas soldiers and 576 home service men, Kofoid and Swezy[3] recapitulated the situation in the United States in the following terms:

(*a*) Carriers of ameba in the United States were greatly increased by the return of the soldiers.

(*b*) There is a larger number of carriers than expected among the normal population.

(*c*) The dysenteric syndrome is not an essential feature of the disease and infection is by no means limited to the tropics.

(*d*) Carrier phases are persistent and are possible foci of contagion.

(*e*) The percentage of carriers relapsing or developing serious sequelæ is unknown.

Without discussion of symptomatology it is still necessary to emphasize some of the characteristic and yet misleading clinical features of chronic amebiasis. The essential lesion in amebic dysentery is an undermining ulceration of the mucosa of the large bowel due to a gelatinous necrosis caused by the invasion of Entameba histolytica. The ameba is not found in the necrotic tissue but ahead of it and invading the healthy submucosa. Under

[1] Jour. Trop. Med. and Hyg., October 15, 1920.
[2] Jour. Am. Med. Assn., August 13, 1913.
[3] New Orleans Med. and Surg. Jour., July, 1920, and elsewhere.

conditions favorable for its growth and reproduction the amebæ exist in a vegetative or free-moving form, while under less luxuriant environment they encyst in a resistant resting form.

The difference between chronic amebiasis and the carrier state is relative only. There is no reason for believing that Entameba histolytica can inhabit the human colon under any circumstances as a mere harmless commensal. If it is in sufficient numbers and is of sufficient virulence to produce clinical symptoms those symptoms may be of most diverse sort. As the infection increases in quantity and virulence the clinical picture will approach that of true dysentery. On the other hand as the infection decreases in quantity and virulence the clinical picture will be that of the carrier state.

Vegetative amebæ as seen in acute dysentery are extremely vulnerable to all manner of hostile influences and consequently die quickly when they have passed from the human host. Moreover, even if ingested vegetative amebæ die from ordinary contact with gastric juice in the stomach. Invasion of man, therefore, is accomplished solely by the encysted form of amebæ. The resistant cysts are carried to the human stomach through the medium of contaminated food or drink, and are only dissolved and the amebæ set free under the influence of the pancreatic juice. It follows that the subacute and chronic cases and the carriers who present no symptoms, and in all of whom cysts are numerous, are alone to be feared from the standpoint of contagion. Vegetative forms are present in proportion to the acuteness of the disease and cysts are correspondingly absent. Fulminating and fatal cases are free from cysts. Chronic cases and carriers have few if any vegetative amebæ, and then usually only in the presence of diarrhea. In the carrier or chronic case an intercurrent diarrhea, as from a cathartic, will be accompanied by the appearance of vegetative amebæ. In these cases, just as occurs in cholera carriers, there is constant risk of some intercurrent factor causing an exalted virulence of the amebæ, for instance, acute mild intestinal indigestion or any temporary lowering of resistance or vitality.

Chronic amebic infection is frequently accompanied by symptoms of a nature so diverse, bizarre or unexpected that no diagnostic help is afforded and amebic colitis is not even suggested. One or more of the following conditions, for example, may occur: Neurasthenia, physical depression, constipation, recurrences or exacerbations, long intermissions, a surprising absence of bowel disorders, more or less decrease of weight, gastrointestinal complaints of great variety, anemia, pain and soreness in the right lower quadrant, chronic dyspepsia, general ill feeling and nervousness. In the cases seen on the Pacific Coast the latent and atypical course is prevalent. Not infrequently after a general examination has failed to reveal the origin of complaints such as those mentioned

amebic cysts are discovered and the symptoms disappear after appropriate treatment.

It cannot be too strongly emphasized that amebic infection is prevalent in the United States, that acute clinical dysentery is far from being a universal feature of it, and that every patient in whom etiologic diagnosis is indefinite or gastrointestinal symptoms are present should be investigated for the presence of ameba. Two chief vectors are concerned in the spread of amebic cysts in the actual transference of cysts from infected dejecta to new mouths. These are water and flies. Moisture may prolong the life of cysts to a month or more, and cysts may be carried directly through the agency of unboiled drinking water or indirectly through the use of infected water in mouth washes, enemas, douches or in cleansing food. Flies do not carry amebic cysts primarily on their feet, which they clean frequently, but through the medium of infected fecal matter eaten and passed again by the fly. The chief danger, therefore, is from fly droppings.

Diagnosis of amebic colitis rests finally and solely on the presence of vegetative Entameba histolytica or its cysts in the dejecta. From a more general point of view two rules can be formulated with safety: The first is to search for amebæ whenever an obscure clinical picture presents itself without definite localization. The second rule is to search for amebæ in every case presenting intestinal symptoms of any sort. Many a patient who has been having his ups and downs for years will clear up when his amebic infection is removed. Under these two general rules diagnosis is much more intimately concerned with thorough routine examination than with discovering a dysentery syndrome. Examination for amebæ should be practised as invariably under these circumstances as examination of the prostate, the rectum and common points of focal infection.

Whenever there is suspicion of colonic disturbance rectal and sigmoidoscopic examination should be instituted at once, and such a routine practice will save many a mistaken diagnosis and many a life. Obviously in a diarrheic or dysenteric condition examination for amebæ and other parasites will be exhaustively prosecuted. Frequently amebæ will be found in direct scrapings from sigmoidal or rectal ulcers or will be found imbedded in mucus secured by the insertion of a soft fenestrated colon tube. In a chronic or latent case microscopic search should include specimens both of a formed and of a liquid stool. The former is more apt to show cysts and the latter, as obtained after salts, is apt to contain vegetative forms. The vegetative forms are more common in the mucus and blood while the cysts are inclined to be found in the firm fecal portions. Negative examinations of three different stools are necessary to establish reasonable certainty of the absence of amebæ. Motile forms should be checked by the dis-

covery of the corresponding cysts. Of the two, cysts are more distinctive than motile amebæ. Herbert Gunn[4] has shown the confusion that may exist between the appearance of pathogenic motile amebæ and that of active fresh leukocytes. This confusion is especially noted in the gall-bladder, bile ducts, abscesses and pus as well as under certain conditions in the colonic contents. A wet smear preparation of normal blood will show these ameboid leukocytes actively motile for many hours. After intensive treatment of amebic colitis the stools should be demonstrated free from amebæ for six months before reasonable assurance of cure is entertained.

The technical methods for the microscopic examination for amebæ are detailed in standard texts and will not be reviewed here. The essential object of the examination is to differentiate the pathogenic Entameba histolytica from the relatively harmless Entameba coli and Entameba nana. More knowledge is required before we can say with finality that these so-called non-pathogenic amebæ are really harmless when they parasitize a human host. So-called cultural or water amebæ are not parasitic for man. Pathogenic properties in amebæ are related apparently to a necessity for living in or on living tissue. Non-pathogenic amebæ feed on waste or other non-living material.

The recently described Entameba nana is often distinguished with the utmost difficulty from Entameba histolytica. Special training and experience are necessary in order to recognize and diagnose amebic cysts just as is the case with vegetative forms. Only the opinion of a trained parasitologist is worthy of confidence. There is reason for believing that pathogenic amebæ may be modified by varying climatic conditions and personal relations of the host into differentiated species.

In differential diagnosis we must remember that amebiasis can only be determined by the presence of pathogenic amebæ. Returning to the classification of dysenteries we have to consider first those of bacterial origin. These are of two kinds: (*a*) Those due to some strain of dysentery bacilli; specific agglutination tests, fever and evidence of toxemia are characteristic of these. (*b*) Dysenteries due to customary intestinal bacteria. Such a primary diagnosis can only be made in the presence of visible ulcerations after scrupulous exclusion of amebæ and dysentery bacilli. Secondarily such a bacterial invasion may follow amebic ulceration and be a potent agent in prolonging the primary lesions. Especially in tropical climates amebic and bacillary dysenteries may be combined, and while improvement may follow specific treatment of the one the patient will not be cured until both have been specifically attacked. It is a principle of tropical practice

[4] California State Jour. of Med., 1921.

that the diagnostician cannot safely rest with the establishment of the first diagnosis arrived at. He must embrace in the technic of his study a review of the entire category of possibilities. This is due to the fact that in chronic and parasitic diseases the diagnosis is apt to be multiple. In no department is this principle more valid than in the diagnosis of dysentery.

Little need be said of the differentiation from amebic colitis of dysenteries of class 2, those due to other specific diseases, such, for instance, as tuberculosis, except to emphasize the constant danger of confusing cancer low in the large bowel with a parasitic dysentery. In temperate climates and in patients over forty years of age, especially if they have not obviously been exposed to parasitic invasion, cancer must be consciously excluded. Chronic amebiasis may be simulated by intestinal tuberculosis, and both are apt to be localized in the cecum and ascending colon.

Dysenteries of the third class, due to toxic substances, are distinguished from amebic colitis by the absence of parasites and by the history and evidences of the causative poison. The same may be said of those due to irritant substances. Dysenteries due to animal parasites other than amebæ depend for their recognition on the discovery of those parasites and recognition of their natural history in man. Combined infections are frequent.

Treatment. The treatment of amebic colitis will be discussed from the standpoint of personal experience only. This experience includes two years' work in central China with foreigners and native Chinese as well as the resources of private practice and the Stanford medical wards. No reference will be made to the enormous literature, history and experimentation on this subject. There is a wide divergence of opinion and practice in the treatment of amebiasis, and the surprisingly large number of patients relapsing after various common methods of treatment is the best commentary on their effectiveness. It can be anticipated that some 90 per cent of chronic cases can be cured along the lines here advocated. Further courses of treatment will reduce the remainder. A residuum will be left as incurable by any method of treatment, and such cases will usually be found to harbor deep-seated infection in the appendix or other remote focus.

Acute Amebic Colitis. In the presence of acute clinical dysentery due to Entameba histolytica the stools show abundant vegetative forms and few if any cysts. Emetin hydrochloride should be administered, 1 gr. in one dose hypodermically daily, for six to eight days. Improvement is usually seen at once and clinical cure seldom requires more than three to five days. From the etiologic and symptomatic standpoint no concomitant treatment is required. But thoroughness of treatment is perhaps enhanced and mixed infections better controlled if the patient is kept warm and absolutely quiet in bed on a restricted smooth diet. After

an interval of two to four days the emetin should be repeated in similar dosage for five days. Following this second course the physician is guided by the results of stool examination, and further treatment, if needed, is substantially as detailed below for chronic cases, omitting the first week. Intravenous use of emetin is seldom necessary and is indicated only in fulminating cases.

Chronic and Latent Amebic Colitis. In the subacute, chronic and carrier stages motile amebæ become progressively fewer and cysts alone are usually found. In the chronic cyst-bearing amebiasis a course of ipecac in massive doses is sometimes first employed. After a day of absolute rest on regular diet a single dose of 90 gr. of powdered ipecac root is administered in 5-grain salol-coated pills. Opium in some form is given a half-hour previously. If possible this dose is increased to a maximum of 120 gr. In no case is this course prolonged beyond five days. Severe diarrhea is frequent and vomiting may appear at any time. It is a matter of judgment how far to modify the treatment in the presence of these or other complications.

After the ipecac course two days of rest on regular diet are allowed. The second week is inaugurated by 0.3 gram neosalvarsan intravenously. Each day, beginning with the neosalvarsan day, a total of 3 gr. of bismuth emetin iodide is given by mouth in one-grain pills. Each evening of this week a colonic irrigation is given with the patient in the knee-chest position. As near as possible to one gallon of 1 to 2000 thymol solution at body temperature is slowly introduced through a soft short colon tube.

The emetin iodide and colon irrigations are continued for six days, and on the seventh the patient rests. On the first day of the third week 0.9 gram neosalvarsan is given intravenously and the emetin bismuth iodide is continued as before for six days. The daily colon irrigation is continued each evening, using 1 to 2000 quinine solution. A third neosalvarsan completes the third week. The value of the colonic irrigations is sometimes debated, but the thoroughness of the treatment is doubtless enhanced by their inclusion. In place of the bismuth emetin iodide emetin hydrochloride may be employed hypodermically.

After the third week ordinarily treatment is contingent on the recurrence of cysts in the stools, in which case the procedure of the third week should be repeated. Stool examinations should be made at least twice weekly for a month, including both liquid and formed specimens, weekly for a second month, and monthly for two additional months before the case is pronounced clinically cured. At the present time it is doubtful if we can state with certainty when amebic colitis is permanently cured. Lacking ipecac treatment in some form the parasites probably remain permanently in man when once established. While there is a

possibility of amebic parasitism being self-limited, as in the case of hookworm, the point is still uncertain.

The title of this paper does not include discussion of complications of amebic colitis. However, mention must be made of amebic foci in the appendix which are probably responsible for many resistant cases. Many of these, uncured by other treatment, will be cleared by appendicostomy and colon irrigation. But the same result apparently follows appendectomy and surgical removal in this way of the amebic focus. Appendectomy, therefore, should be considered in cases resistant to medical treatment. Biliary tract infection is a possibility worthy of serious consideration.

Prevention of Amebiasis. Obviously prevention of amebic infection depends primarily on proper disposal of cyst-infected fecal material. Secondarily and more practically it depends on avoidance of ingestion of cyst-infected food and drink. Food infection is favored chiefly by flies and by unclean methods of handling and preparation. Every individual should make it a practice to wash his hands immediately before eating and to keep his fingers out of his mouth at all times. In a broader sense, too, the introduction of pathogenic amebæ by foreign immigration deserves special concern.

Emetin. Emetin is a potent and toxic alkaloid and must be handled circumspectly. It causes gastrointestinal irritation, low blood-pressure with a fast, weak heart and depression of the central nervous system. Its toxicity varies with different commercial preparations. The diarrhea produced by emetin may be confused with an uncured dysentery, and serious poisoning result, from pushing the drug too far. Occasionally cases of idiosyncrasy to emetin are seen. It causes considerable local irritation on injection. The use of emetin has been discussed in greater detail previously.[5]

Conclusion. In the words of Manson, "The capacity for latency often exhibited by the germs of dysentery is remarkable." Pathogenic amebæ are widely spread in the United States. Because of their tendency to produce carrier and chronic forms the physician should be constantly on the watch. Atypical, unexpected and bizarre symptoms are surprisingly frequent. Diarrhea and dysentery are frequently not present either in the history or present status of patients suffering from amebic colitis. No obscure case has been sufficiently studied until amebæ have been eliminated as a possible cause, and every gastrointestinal case, in its diagnostic routine, should have included a search for these organisms.

[5] Reed, Alfred C.: Boston Med. and Surg. Jour., September 14, 1916.

REVIEWS.

COLLECTED PAPERS OF THE MAYO CLINIC. Edited by Mrs. M. H. MELLISH. Vol. XIII, 1921. Pp. 1318; 392 illustrations. Philadelphia and London: W. B. Saunders Company, 1922.

EACH annual volume from the Mayo Clinic since 1914 confirms the opinion expressed in this journal by the reviewer (A. P. C. A.) of the *Collected Papers* of that year to the effect that the Clinic was then entering upon its third and final period of development, a period characterized by an "interest which centers in pathology—the causes and natural course of disease." Only 4 of the 117articles included in this volume are listed under the heading of technic (first period) and very few relate to the end-results of surgical treatment (second period), whereas the great majority concern themselves with the development and course of disease. In order to further this end, not only have extensive clinical investigations been made but much experimental work on lower animals has been accomplished. Thus the Mayo Clinic now stands for the investigation of disease from the broadest scientific point of view. The articles as a whole are well written, make ample reference to the literature, are splendidly illustrated and in number probably exceed the total product of any other local medical organization.

T. G. M.

VITAL FACTORS OF FOODS. By CARLETON ELLIS, Consulting Chemist, and ANNIE LOUISE MACLEOD, Associate Professor of Chemistry, Vassar College. Pp. 391; 12 illustrations. New York: D. Van Nostrand Company, 1922.

THIS book is one of the most complete and comprehensive offerings that has appeared on the subject of vitamins. The first part of the book is taken up with their historical development, followed by a series of chapters on their nature, classification, distribution and stability; while the latter part is devoted specifically to the deficiency diseases, especially from the point of view of the pediatrician. An extensive table on the distribution of vitamins is included in the appendix.

The outstanding feature of the book is its completeness and its magnificent bibliography. The organization of the material also

warrants special comment. The personalities of the authors are, however, completely submerged, and there is a lack of the critical element. The book partakes more of the nature of a collection of abstracts of the work and opinions of the investigators in this field of nutrition, leaving the reader more or less to formulate his own conclusions.

While the book does not present any previously unpublished material, it must, nevertheless, be considered a distinct contribution to the science of nutrition. The investigator will be delighted with the splendid set of references, while the dietitian, the pediatrician, and the general practitioner will find it a ready and up-to-date handbook. A. J. Q.

THE PSYCHIC HEALTH OF JESUS. By WALTER E. BUNDY, Ph.D., Associate Professor of English Bible in DePaw University. First edition. Pp. 299. New York: The Macmillan Company, 1922.

To most people the mere intimation that the psychic health of Jesus was not normal appears as sacrilege, yet the author has undertaken the task of discussing this subject chiefly in reply to certain articles and books which have been published in German and in French, articles that have pointedly discussed the psychic health of Jesus and in which the authors concluded that Jesus was of unsound mind.

The psychic health of Jesus is discussed by some of his critics under various headings, such as: "Was Jesus an epileptic?" "Was Jesus a paranoiac?" "Was Jesus an ecstatic?" "Was Jesus a fanatic?" None of his critics make mention of the possibility of Jesus having been a sufferer from manic-depressive insanity, despite the fact that there is apparently a clear history of mental disease in his family. His relatives and friends, as recited in *Mark*, 3:21, evidently believed that Jesus was of unsound mind. This verse says, "And when his friends heard it, they went out to lay hold on him: for they said, He is beside himself." On this particular paragraph in *Mark*, Soury has commented as follows: "If Mary and the brothers of Jesus had brought him again into the house of the carpenter of Nazareth, the Galilean prophet would perhaps have ended his life obscurely in some cellar of the paternal dwelling, held by a chain as a Gadarene demoniac." "The Transfiguration," "The Cursing of the Fig Tree," "The Cleansing of the Temple" and Jesus' attitude toward his mother are all additional evidence to those who believe that Jesus was of unsound mind.

The author, in a whole-hearted manner in which his faith is evident, endeavors to refute the arguments put forward by Jesus' critics. The book has an absorbing interest and should be widely read. G. W.

THE PRINCIPLES OF ELECTROTHERAPY AND THEIR PRACTICAL APPLICATION. By W. J. TURRELL, Consulting Physician, Oxford County and City Mental Hospital. First edition. Pp. 276; 29 illustrations. London: Henry Frowde, Hodder & Stoughton, 1922.

THIS small book is divided into four parts. In Part I current electricity is discussed; Part II is devoted to the task of explaining the therapeutic action of radiant energy; Part III is concerned with electrodiagnosis; the last subdivision of the book explains the action of electrotherapy and some of the conditions for which it is used and also gives the indications for electrical treatment. This last part has to do largely with the ordinary uses of electricity.

This book, while not an exhaustive treatise, presents the subject in a clear and concise manner and should be of value to anyone who uses electricity in his practice. G. W.

STUDIES IN INFLUENZA AND ITS PULMONARY COMPLICATIONS. By D. BARTY KING, O.B.E., M.A., M.D. (Edin.), M.R.C.P. (Lond. and Edin.), Physician to the Royal Chest Hospital, London; Consulting and Examining Physician to the Church Army Sanatorium for Children Suffering from Pulmonary Tuberculosis, Fleet, Hants. Pp. 88; 31 illustrations. New York City: Paul B. Hoeber, 1922.

THIS attractive little book consists of three studies in influenza made by the author while in charge of the medical division of the County of London (Horton) War Hospital during the late war. The first of these has to do with an outbreak of the epidemic among 150 cases of malaria, the second with the after-effects of the acute pulmonary complications of influenza as revealed by clinical roentgenoscopic and postmortem examinations, and the final one with the disease as it affected the nursing staff (329) of the hospital. Numerous case reports, temperature charts, tables and diagrams of chest physical findings and of roentgenoscopic results are included, and serve to greatly enhance the value of the work. The importance of getting the patients to bed promptly is emphasized and strophanthus is the drug which he believes most helpful when pulmonary complications arise. A plea is made for repeated clinical and roentgenoscopic examinations of pneumonia patients during their convalescence in order to discover in their early stages the various complications which, unless properly treated, may end in chronic fibroid lung disease. The chief treatment advocated for this type of affection is respiratory exercises.

T. G. M.

THE CLINICAL METHOD IN THE STUDY OF DISEASE. By R. M. WILSON, M.B., Ch.B., Consulting Physician to the Minister of Pensions. Pp. 57. London: Henry Frowde, Hodder & Stoughton, 1921.

IN the scope of an hour's reading there is presented a brief sketch of the life and works of Dr. Horace Dobell, followed by an interesting discussion of the method of study practised by that eminent clinician of the last century and the conclusions to which his studies led him. J. H. A.

HYPERPIESIA AND HYPERPIESIS. By H. BATTY SHAW, M.D., F.R.C.P., Physician to University College Hospital and to the Brompton Hospital for Diseases of the Chest. Pp. 191; 11 figures and 53 charts. London: Henry Frowde, Hodder & Stoughton, 1922.

FIFTY cases of hypertension which have come to autopsy furnish the material upon which this study is based. An outline of the history, physical examination and autopsy findings is given in the first section of the book. The remaining sections are devoted to analysis of the preceding findings, deductions which may be drawn therefrom and experiments and speculations concerning the cause of hyperpiesia. Pathologic studies of the injected kidneys by Lawrence and the systolic blood-pressure charts which accompany each case-history constitute an important feature of the work and make it worthy of examination. No chemical tests of kidney function are recorded in connection with any case, although admittedly nephritis and diminished kidney function are of primary importance in connection with hyperpiesia. The omission of these and other modern diagnostic methods detracts seriously from the value of the book. J. H. A.

SMELL, TASTE AND THE ALLIED SENSES IN THE VERTEBRATES. By G. H. PARKER, Professor of Zoology, Harvard University. Pp. 192; 37 illustrations. Philadelphia: J. B. Lippincott Company, 1922.

SINCE the so-called higher senses, sight and hearing, have so much to do with our mental states many works have appeared summing up our knowledge of those senses at different times; in comparison, the other senses have been quite neglected. The present work is an attempt to fill this need as far as it concerns the chemical senses, senses which have so much to do with the proper

functioning of our alimentary tract. Taste and smell both having receptors of chemical stimuli form a very natural group.

Through human examples the author introduces each sense, both in the morphology of the receptors and in their physiology, finally pointing out the situation as it occurs in other animals. The author's great experience in the comparative physiology of the sense organs particularly well fits him to discuss this aspect of the subject. The concluding chapter of the book includes the relation of one sense organ to another and proposes a terminology to deal with sense organs in general, a terminology more or less familiar to one already acquainted with the work of the author.

The editors of the "Monographs on Experimental Biology," of which this is one of the series, have done well in selecting Professor Parker to present these important subjects. H. S. C.

AN INDEX OF TREATMENT BY VARIOUS WRITERS. Edited by ROBERT HUTCHINSON, M.D., F.R.C.P., Physician to London Hospital and to the Hospital for Sick Children, and JAMES SHERREN, C.B.E.,F.R.C.S., Surgeon to the London Hospital and Consulting Surgeon to the Poplar Hospital for Accidents. Revised to conform with American usage by WARREN COLEMAN, M.D., Assistant Professor of Medicine, University and Bellevue Hospital Medical College; Visiting Physician to Bellevue Hospital. Eighth edition, revised and enlarged. Pp. 1029; 88 illustrations. New York: William Wood & Company, 1922.

THIS revised edition is printed on a larger page and plainer type than its predecessor. It is thus unified in all particulars with the two companion volumes of this same series—the *Index of Differential Diagnosis* and the *Index of Prognosis*. It aims to provide the practitioner with a complete guide to treatment in one volume. The list of contributors is entirely British and therefore the suggested methods of treatment are not always in accord with American practice. For this edition revision by the American editor consists in adopting various prescriptions to the standards of the *United States Pharmacopeia;* sometimes he comments on the British text in some added footnotes.

The first volume of this work appeared in 1907. Each succeeding effort has profited by the omissions and mistakes of previous editions; so that the present one reaches the high-water mark. The articles on burns, diabetes, electrotherapeutics, hysteria, mental diseases, neurasthenia and rabies have been rewritten, while new ones on encephalitis, kalaazar, snake-bite, transfusion and the surgical treatment of constipation have been added.

It is, of course, no difficult matter to still find omissions according to American ideas, and it is easy to point out suggestions made

which have no real place in the various therapeutic fields. This would be unfair because the book is primarily written for the British by British and for them it is the foremost work of its kind. It is a book that must be useful to every one who studies or practices medicine, because it offers quickly and briefly the important treatment of all conditions, alphabetically arranged, from abdominal injuries to zomotherapy. T. G. S.

GLANDS IN HEALTH AND DISEASE. By BENJAMIN HARROW, Ph.D., Associate in Physiologic Chemistry, College of Physicians and Surgeons, Columbia University. Pp. 218; 2 illustrations. New York: E. P. Dutton & Company, 1922.

THIS book represents an effort to place before the laity a simple statement of the known facts about the endocrine glands. The author cannot resist the temptation to theorize a little, however, though he is careful to explain that he is doing so. It is the sort of book a clinician, rather than a laboratory man, should have written. The former would not have been so pessimistic about the surgical treatment of exophthalmic goiter, would not have declared that endemic goiter represents a thyroid hyposecretion as "is made evident by the general symptoms that develop," and would have devoted less space to such things as Steinbach's and Voronoff's methods of imparting vigor to the body by operations on the genital apparatus, or grafting. T. G. M.

EPIDEMIOLOGY AND PUBLIC HEALTH. A Text and Reference Book for Physicians, Medical Students and Health Workers. In three volumes. Volume I, RESPIRATORY INFECTIONS. By VICTOR C. VAUGHAN, M.D., LL.D., Chairman of the Division on Medical Sciences of the National Research Council and Emeritus Professor of Hygiene in the University of Michigan; assisted by HENRY F. VAUGHAN, M.S., Dr. P.H., Commissioner of Health of the City of Detroit, and GEORGE T. PALMER, M.S., Dr. P.H., Epidemiologist for the Department of Health of the City of Detroit. Pp. 688; 83 illustrations. St. Louis: C. V. Mosby Company, 1922.

WHEN the reviewer received this book he anticipated no special pleasure in the reading of it, but the first paragraph of the preface, in which the author tells of the vivid impression made upon his boyhood mind by the recurring epidemics of "bloody flux" in Missouri, and the subsequent paragraphs in which he relates in brief outline his vast personal experience with epidemic disease, were sufficient assurance that not only might one expect a presentation based upon and tempered by a knowledge gained at first

hand, but one that emanated from a large human interest. In both of these respects this first volume proves itself a complete success.

It is far more than a mere accumulation of statistical data on epidemic disease, though in this regard alone it is of great value, for it brings into permanent and orderly form much important matter from our recent war experience. But besides this the history of epidemic disease, which is always interesting, is dealt with, and also the symptomatology and pathology. Furthermore, the authors have emphasized their personal views in regard to the phenomena of infection, and this in itself tends to give to the book a decided point of view. This is evidenced by the heading for the first chapter—Albuminal Diseases. Other chapters are devoted to individual diseases, as measles, influenza, tuberculosis, etc. Consequently the treatise is of great value to internists generally, as well as to those especially interested in public health. The tables and charts are well prepared and most illuminating. The reviewer will eagerly await the subsequent volumes. T. G. M.

STUDIES IN NEUROLOGY. By HENRY HEAD, M.D., F.R.S. In two volumes. Pp. 832; 182 illustrations. Oxford Medical Publications, Oxford University Press, 1920.

THIS scholarly work is in two volumes and is essentially a republication in an orderly review of a series of seven papers published from 1905 to 1918 inclusive by the author in conjunction with W. H. R. Rivers, James Sherren, Gordon Holmes, Theodore Thompson and George Riddock. No material change has been made in the arrangement of the papers, as each of them deals with a definite theme and is concerned with some distinct aspect of the functions of the nervous system. The author has also added an introduction and an epilogue dealing with the common aims which underlie the various researches, and an appendix dealing with some of the most serious criticisms of the researches on the functions of the peripheral nervous system.

The two volumes are noted for the extreme care and precision used in testing the sensory tracts of the peripheral nervous system, the spinal cord and the brain. The author submitted himself to an experimental section of a cutaneous nerve of his arm and subsequently made many very careful and consecutive notes concerning the resultant sensory changes and those consequent upon the gradual regeneration of the nerve. The first volume is devoted to a discussion of the methods of examination and their trustworthiness particularly as applied to the peripheral nervous system. The second volume deals principally with the spinal cord and the brain and particularly with those sensory disturbances resulting from cerebral and spinal cord lesions.

The book is one of the most scientific and trustworthy that has appeared on the market in recent years and while it advocates no new departure from the realms of organic neurology, it sheds much new light on many obscure facts concerning cerebral and spinal localization, especially as viewed from the angle of the doctrine of evolution. The authors trace physiologic processes produced by various physical stimuli from their origin at the periphery of the nervous system to the moment when they excite sensation.

The leading principles which have emerged from these researches are:

1. When any level of activity is attacked the most complex functions, and those which have appeared most recently in the scheme of human development, are the first to suffer.

2. The negative manifestations of a lesion appear in terms of the effected level, and a negative lesion produces positive results by releasing activities normally held under control by the functions of the affected level.

3. The functions of the central nervous system have been slowly evolved by a continuous process of development.

4. Integration of function within the nervous system is based on a struggle for expression between many potentially difficult physiological activities.

5. Primitive sensation was probably a condition of "awareness" endowed with but slight qualitative or discriminative characters.

The book may be considered as a classic of its kind and is a valuable addition to the library of the neurologist. F. H. L.

VENEREAL CLINIC. By ERNEST R. T. CLARKSON, M.R.C.S., London Hospital. Pp. 456; 35 illustrations, 20 plates (10 in color). New York: William Wood & Company, 1922.

IN the wealth of books of this character, at present on the market, it hardly seems possible to expect anything new. Yet the author has given it to us, not essentially in the material contents, but in the presentation of his subject. Covering only the two diseases, gonorrhea and syphilis, he has presented the subject-matter: (1) As seen in their most frequent manifestations; (2) as though demonstrating individual cases at a clinic; (3) by closely correlating the symptoms with the known pathology and reasons for certain treatments, and enhancing the value of the whole by appending a splendid series of chapters on the sociology and administration of clinics and city health measures. He has written for the "elementary student" and the practitioner taking charge of a venereal clinic: to both we take pleasure in warmly recommending the book, judging it to be safe in its advice, clear in its presentation of the subject and easy of ready reference, with many additional features not found elsewhere. A. R.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND

ROGER S. MORRIS, M.D.,

FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO,

AND

THOMAS ORDWAY, M.D.,

DEAN OF UNION UNIVERSITY (MEDICAL DEPARTMENT), ALBANY, N. Y.

Megacaryocytes in Circulation.—MINOT (*Jour. Exper. Med.*, 1922, **36**, 1) reports the finding of megacaryocytes (megalocaryocytes) in the peripheral circulation of many cases of myelogenous leukemia and in two cases of polycythemia vera, one of lobar pneumonia, one of Hodgkin's disease, and one of sepsis. In all of these cases, except some of the myelogenous leukemias, the blood showed increase of platelets with bits of megacaryocyte cytoplasm and often many immature cells of both the red and white series. The author concludes that the presence of megacaryocytes in the peripheral circulation is indicative of a bone-marrow under intense strain.

The Blood Sugar After Removal of the Liver.—MANN AND MAGRATH (*Arch. Int. Med.*, 1922, **30**, 73) report their observations on the blood sugar in hepatectomized dogs as an interesting phase of their studies on the physiology of the liver. The technic of the removal of the liver includes, first, a reverse Eck fistula and, at the second operation, the ligation of the portal vein at its entrance into the liver, the third operation allowing the removal of the entire liver. Following the operation the animal remains "normal" for three to eight hours and then passes through a series of symptoms—muscular weakness, loss of reflexes, flaccidity, return and exaggeration of reflexes, muscular twitchings, convulsions and death. The average animal dies within two hours after the appearance of the first signs of muscular weakness. The authors point out that the blood sugar begins to fall immediately after operation and its fall to a certain point (0.06—0.04 per cent) is always

accompanied by the onset of the symptoms described. At the time of death the blood sugar rarely exceeded 0.03 per cent. The glycogen content of the muscle decreases coincidently. Similar studies were made on animals of different species—dog, goose, turtle and fish. In each species investigated removal of the liver produced a marked decrease in blood sugar. The relationship, they conclude, of the decrease in blood sugar and the development of the characteristic symptoms seems to be one of cause and effect.

Capillary Blood-pressure in Arterial Hypertension.—Boas and Frant (*Arch. Int. Med.*, 1922, **30**, 40) find that hypertension cases fall into two groups, (*a*) those with normal capillary blood-pressures, and (*b*) those with high capillary blood-pressures (21–70 mm. of Hg). They agree with Kylin that it is possible that the patients who exhibit high capillary pressures are suffering from a general capillary disease with a glomerulonephritis as one of the manifestations, although they point out that it is difficult to see how disease of the capillaries themselves would lead to a high capillary pressure, particularly when arteriosclerosis of itself does not lead to a high arterial pressure. In cases of essential hypertension the capillary pressure is low. They find that in patients with high capillary pressure the variation in different capillaries of the same patient is twice as great (36.6 mm. Hg) as in patients with normal capillary pressure (18.0 mm. Hg). They also conclude that the variability of the capillary pressure depends on physiologic as well as anatomic moments.

Studies on Blood Cholesterol in Syphilis.—McFarland, (*Arch. Dermat. and Syph.*, 1922, **6**, 39) has studied the cholesterol content of the blood in a number of syphilitic patients and finds that in general the values are medium and low rather than high. The cholesterol determinations, done by the Bloor method, are, with the possible exception of cases of cerebrospinal syphilis, about the same as in a similar series of non-syphilitic individuals. In cerebrospinal syphilis the percentage of high values was 33.3. The possible relationship between the cholesterol values and the Wassermann reaction, the type of syphilis, and the clinical response to treatment were also studied with negative results. It is of particular interest to note that the positive Wassermann reaction depends in no way on the concentration of cholesterol in the blood. The blood of patients under treatment was also studied with the idea of determining the possible effect of arsphenamine. Here again no significant variations were noted.

The Role of Agglutination in the Immediate Toxic Effects of Arsphenamine.—Oliver and Yamada (*Jour. Pharm. and Exper. Therap.*, 1922, **19**, 393) in a series of interesting experiments on animals demonstrated that when single large lethal doses of arsphenamine are given, a characteristic anatomical finding is present in animals at autopsy. This consisted in marked agglutination of the blood from the inferior vena cava, which is definitely shown not to depend on coagulation; as a result of this phenomenon, embolism of small vessels and capillaries throughout practically all the organs and particularly in the lungs. They were also able to demonstrate that rabbits died acutely from the intravenous injections of red cells previously agglutinated by arsphen-

amine in vitro, in which the arsphenamine content was much too low to have caused symptoms. The clinical and anatomical phenomena in these animals were precisely the same as in animals killed with a single large dose of the drug. Similar reactions of a less extent occurred after large sublethal doses of arsphenamine and after small repeated doses. They call attention to the fact that sudden death in the animal depends on the almost complete stoppage of the pulmonary capillaries by embolism and that this in turn causes an acute dilatation of the right ventricle. They suggest that certain of the similar reactions observed in human beings may be due to the intravascular agglutination of the red cells and the consequent multiple embolism.

A Serological Study of Hemolytic Streptococci.—GORDON (*Brit. Med. Jour.*, 1921, **1**, 632) has studied by means of agglutination and absorption tests hemolytic streptococci derived from a variety of sources with special reference to the organism concerned in scarlet fever. It is found that of a large group of streptococci, 93 per cent fell into three main serological types. Of special interest was the fact that in the scarlet fever cases all but two strains were identical and these two strains were different from those obtained in ordinary pyogenic conditions. These observations confirm the work of Bliss and of Tunnicliff and raise the question of whether the steptococcus may not really be the actual cause of scarlet fever. Its constant presence even early in the disease, and the fact that if one eliminates the streptococcus and its associated rash very little remains from which to make a diagnosis, are very suggestive.

Remote Prognosis in War Nephritis.—DYKE (*Quart. Jour. Med.*, 1922, **59**, 207) analyzes the present condition of 100 patients whom he observed in the acute stage of war nephritis four and a half years ago. All had been typical cases of acute nephritis with edema, albuminuria, and hematuria. His observations have a significant bearing on the problem of nephritis in civil life. Of 100 patients followed, 3 are dead, 1 is a complete invalid, 17 are partial invalids with pensions of 20 to 60 per cent, and 79 are "fit." Most of these now found to be fit for duty were completely recovered within twelve months of the onset of the acute disease. Most of those not fully recovered within twelve months have persistently shown signs of nephritis, which by this time is of the chronic type. Eleven patients recovered more slowly and although invalid at one year after the onset have since so far recovered as to be capable of full duty. No symptom or sign (including uremia) occurring during the acute stage of the disease was found to be a reliable guide to its remote prognosis.

Radium Emanations in Exophthalmic Goiter.—TERRY (*Jour. Amer. Med. Assn.*, 1922, **79**, 1) used radium emanations in extremely toxic cases of exophthalmic goiter in an attempt to convert them into better risks for surgical procedures. The emanation tubes were introduced into the gland under local anesthesia. Two patients with high metabolic rates recovered completely after radium alone. Other cases were so far improved as to be favorable subjects for operation. The adhesions which are reported to follow preparatory treatment with the roentgen-ray were not observed in patients treated with radium.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

. **Thoracoscopy in Surgery of the Chest.**—JACOBAEUS (*Surg., Gynec. and Obst.*, 1922, **34,** 289) says that for diagnosis and localization of pleural and pulmonary tumors it is of great importance to make a roentgen-ray examination before as well as after the induction of pneumothorax. By making a roentgen-ray examination after the induction of pneumothorax, valuable information is obtained which completes the information already obtained by the roentgen-ray examination before the induction of pneumothorax. Thoracoscopic examination gives valuable information in diagnosing and localizing pleural and pulmonary tumors and verifies the roentgen-ray examination. If it is not possible to use a pressure difference apparatus, it might be advantageous to induce pneumothorax previous to operation in the pleural cavity. If a pressure difference apparatus be employed, then pneumothorax for the thoracoscopic examination ought to be induced as shortly before the operation as possible, in order that the inflation of the lung after the operation may not be rendered more difficult or impossible. If the lung is inflated after the operation, more favorable conditions for the course of healing are eventually obtained.

Gross Pathology of Brachial Plexus Injuries.—ADSON (*Surg., Gynec. and Obst.*, 1922, **34,** 351) says that injuries of the brachial plexus are chiefly situated in the vicinity of the intervertebral canal proximal to the brachial trunk. The injuries may be slight, lacerating only the fascia around the cervical roots or they may be severe and result in laceration of the cervical roots between the cervical ganglion and the cervical trunk with or without avulsions of the ganglion. Inasmuch as injuries of the brachial plexus are produced in the root or the ganglion, they seem primarily to be lesions of the nerve rather than secondary to lesions of the shoulder joint. Patients with milder injuries may be expected partially or completely to recover without surgical treatment, but those with more severe injuries rarely recover even with surgical treatment.

Surgical Anatomy of the Trigeminal Nerve.—KANAVEL and DAVIS (*Surg., Gynec. and Obst.*, 1922, **34,** 357) say that the distance from a point upon the inner surface of the squamous portion of the temporal bone opposite the preglenoid tubercle to the foramen spinosum was found to average 2.47 cm. There are six distinct types of middle meningeal arteries, the larger percentage of which give off single anterior and posterior branches. The distances from the foramen

spinosum to the Gasserian ganglion, foramen ovale and foramen rotundum respectively are 1.66 cm. at an angle of 20 degrees occipitad from a transverse diameter through the foramen spinosum. In 41 per cent of the cases a marked bony prominence overhangs the foramen spinosum which leads to difficulty in elevating the dura mater and ligating the middle meningeal artery. Further, in 38 per cent marked lateral grooves are present which may lead to difficulty in localization of the operative field. An attempt should be made to save the motor root which lies medial to and somewhat superior to the sensory root centralward from the ganglion. A thin membrane lies between the Gasserian ganglion and the carotid artery in 40 per cent of the skulls examined. The cause of the paralysis of the seventh nerve which infrequently occurs cannot as yet be definitely stated.

Secondary Parotitis.—LYNN (*Surg., Gynec. and Obst.*, 1922, **34**, 367) says that more attention should be paid to the condition of the mouths of our patients before and after operation. Following operations some mild salivary stimulant should be given to keep the ducts clean. The reason the sublingual and submaxillary glands are practically immune is because they are mucous glands, mucin inhibiting bacterial growth. Furthermore, the parotid is the only salivary gland containing lymph glands. These favor the collection of inflammatory agents. There are two main sources of infection: through the blood or lymph stream and by way of Stensen's duct.

A Study of Sixty-five Cases Seeking Relief After Short-circuiting Operations.—SPRIGGS and MARXER (*Brit. Med. Jour.*, April 15, 1922, p. 546) say that about half the patients who sought relief after gastroenterostomy recovered from their symptoms or improved greatly with lapse of time and suitable medical treatment. In most of the remainder a detailed investigation showed abnormalities which are capable of relief by further operation. The conditions which call for a second operation are the persistent failure of medical treatment and inability of the patient to lead a normal life; particularly if it can be demonstrated that bile is regularly in the stomach or that the stoma is not in the lowest part, causing accumulation of food between the stoma and the pylorus, or that the jejunal loops are not normal in appearance, or that there is dilatation of the duodenum and regurgitation of bile, or if there is evidence of ulceration in the neighborhood of the stoma or of active ulceration of the stomach or duodenum. Except for structural disease, short-circuiting operations upon the colon should not be performed unless suitable and persistent medical treatment has failed and sound scientific reasons can be put forward for believing that the operation will benefit the patient. In all cases of chronic alimentary disease, treatment and especially operative treatment should not be undertaken until the case has been investigated as thoroughly as the circumstances permit.

Ascending Infections of the Kidney.—WALKER (*Lancet*, April 8, 1922, p. 684) says that organisms may also reach the kidney by the lymphatics surrounding the ureter and between its muscular coats, although the blood-stream is the commonest route. The kidney capsule is an

important link in this lymphatic chain and is the situation in which organisms are most consistently found in cases of ascending infection. In early cases of lymphatic infection of the kidney no organisms are found in the urine. There are reasons to believe that a tuberculous infection of the kidney may take place along a route precisely similar to that followed by pyogenic organisms.

Gastric Syphilis.—GALLOWAY (*Brit. Med. Jour.*, February 11, 1922, p. 217) says that there are two symptoms and three signs. The symptoms are, first, anorexia—no other condition shows this so absolutely excepting in some early cases of malignant disease, and secondly, the nature of the pain. The signs are, first, enlargement of the liver (and occasionally also of the spleen) with smooth outline, present in three-fourths of all the cases; secondly, rapid development of cachexia; and thirdly, stigmata of syphilis. The real test is the empiric, the therapeutic, and that may be applied both from its negative and positive aspects. The change is immediate upon specific treatment, while the result is *nil* upon mere careful arrangement of diet and usual drugs.

Nature and Cause of Old-age Enlargement of the Prostate.—WALKER (*Brit. Med. Jour.*, February 25, 1922, p. 297) says that it is impossible to explain enlargement of the prostate by any theory of chronic inflammation alone. Although the enlargement may reproduce conditions favorable to the development of a neoplasm, the enlargement itself does not come into the category of true tumors. The condition is in the nature of a fibroepithelial degeneration which finds its analogy in the female in serocystic disease of the breast. This degeneration may be regarded as an accident occurring during the progress of involution of the genital tract. The cause that determines the onset of the condition is unknown, although it is not improbably connected with a loss of endocrine balance occurring during this period. Prostatic enlargement shows a definite distribution that is anthropological rather than geographical in character. It very rarely occurs among Mongolians and negroes.

Anomalous Abdominal Membranes.—TAYLOR (*Ann. Surg.*, 1922, **75**, 513) says that anomalous membranes are present in from 15 to 20 per cent of newborn infants. They result from atypical peritoneal fusion during fetal life. Many of them are probably modified by later pathological changes due to continued traction, irritation or low-grade inflammation. They occur in the hepatoduodenal region, at the duodenojejunal angle and about the cecum, ascending colon, hepatic flexure and beginning transverse colon. They cause mechanical disturbances, fixation, angulation, compression and torsion of the digestive tract, resulting in partial, continuous and often increasing obstruction. This, in turn, frequently causes dilation proximal to the obstruction. Symptoms result when the obstruction becomes greater than the peristaltic efficiency can easily overcome, independently of time of life. The symptomatology consists of digestive disturbances, general nutritional disturbances and nervous debility. There are usually tender spots in the mid-epigastrium, over the appendix, over cecum and ascending colon and over the duodenojejunal angle, depending upon the

presence of the various lesions. Examination of gastric contents and stools gives no evidence of value as a rule. Good series of plates from barium gastrointestinal studies are likely to show hepatoduodenal membranes, duodenojejunal angle obstructions and pericolic membranes.

Clinical Aspects of Abdominal Tuberculosis.—MORLEY (*Brit. Med. Jour.*, March 11, 1922, p. 383) says that pain, when it occurs in recurrent, well-defined, colicky attacks, especially if they return with regular periodicity and sharp intensity, signifies a mechanical interference with intestinal peristalsis and this can be relieved only by operative measures. Glandular masses in the mesentery, if not too extensive and if they do not yield rapidly to constitutional treatment, should be excised and this is particularly urgent when they are associated with colicky attacks of pain. Palpable masses in the ileocecal region associated with signs of chronic intestinal obstruction are an emphatic indication for laparotomy and resection of the tuberculous ileocecal region should such be found. The ascitic form of tuberculous peritonitis is essentially a disease for surgical treatment. The operation is free from danger and its beneficial results are usually dramatic. Finally, in the plastic type of tuberculous peritonitis, if the trouble does not yield to the ordinary medical measures, operation may be undertaken with a fair degree of safety provided that no extensive attempt is made to separate adhesions and there is some ground for hoping that even these apparently desperate cases may make a complete recovery.

The Treatment of Surgical Tuberculosis with the Carbon-arc Lamp.—SAUER (*Ann. Surg.*, 1922, **75**, 400) says that the treatment consists in placing the patient before the light and exposing the affected part and as much of the surrounding area of the body as possible. About eight to ten hours after the first treatment a deep erythema is noticed. It is as effective as the natural sunlight and has the advantages of convenience and independence of the weather. It is just as effective, if not more so than the roentgen ray without the attendant dangers. It is far more effective than the quartz-mercury vapor lamp, as has been amply demonstrated by Reyn.

Tuberculous Abscesses of the Chest Wall.—AUCHINCLOSS (*Ann. Surg.*, 1922, **75**, 406) says that tuberculous abscesses of the chest wall are frequent enough to be of importance to the general surgeon, yet rare enough for many surgeons not to have had enough cases for study as to their pathogenesis and treatment. There is a widespread opinion that such cases are due to a "tuberculous rib" as the distributing or primary focus. From this study the lungs, pleura and the mediastinal lymphatics seem preëminently responsible. The abscess is frequently deep as well as superficial to the chest wall. The abscesses occur chiefly on the anterolateral aspects of the chest wall rather than posteriorly. The associated tuberculous lesions are varied in number and importance. They may be or may not be more important than the abscesses. An extraordinarily large amount of calcium deposit may be present. Complete excision of the tuberculous focus, leaving vascular, well-nourished walls to come together, is the treatment; this may have to be modified by an associated lesion.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

Acute Infectious and Contagious Diseases in Childhood in the Etiology of Cardiovascular Disease in the Adult.—SIEGEL (*Arch. Pediat.*, 1922, **39**, 314) reviews data collected in the examination of recruits for army service. In a series of 74,130 examinations, 6034 were given detailed cardiovascular examination, and 297 were rejected as unfit because of cardiovascular abnormalities. The histories of the last group were taken with special attention to determining the occurrence of measles, pertussis, scarlet fever, diphtheria, rheumatism, chorea, tonsillitis, growing pains, typhoid fever, dysentery, pneumonia, malaria and syphilis. The cardiovascular abnormalities found in the 297 cases rejected occurred as follows: Hyperthyroidism in 99 cases; combined valvular lesions in 61; functional cardiac disorder in 47; mitral stenosis in 35; mitral insufficiency in 20; aortic insufficiency in 10; cardiac hypertrophy in 10; tachycardia, auricular fibrillation, and aortic syphilis in 4 each; bradycardia, auricular flutter, and congenital heart lesion in 1 each. The etiological factors giving rise to these lesions follow in the order of frequency of incidence: Measles in 61.6 per cent; pertussis in 41.75 per cent; rheumatism in 41.4 per cent; tonsillitis in 36.4 per cent; growing pains in 25.3 per cent; pneumonia in 17.8 per cent; typhoid fever in 16.2 per cent; there was no history obtainable in 14.1 per cent; scarlet fever in 12.8 per cent; diphtheria in 11.9 per cent; dysentery in 11.1 per cent; and chorea in 5.4 per cent. It seemed that diseases causing the gravest constitutional symptoms in this series showed a lower incidence of cardiovascular damage than those in which the constitutional reaction was milder, and in which the patient is either ambulant or in bed for comparatively a short period. This would seem to indicate the danger to the circulatory apparatus following an infectious disease and should emphasize the need of keeping children, ill with these diseases, at rest not only during the period of the acute attack, but also in the post-acute stage, until the circulatory system has returned to its normal state. This should considerably aid in the avoidance of permanent damage to the circulatory system.

Results of Active Immunization with Diphtheria Toxin-antitoxin in the Public Schools of New York City.—ZINGHER (*Jour. Am. Med. Assn.*, 1922, **78**, 1945) reports that the immunity response to the same mixture of toxin-antitoxin varies greatly in different groups of children. A preliminary stimulation of the tissue cells in Schick-positive children caused by repeated exposure to infection with the diphtheria bacillus seems to enable the cells to give a better response to injection of toxin-antitoxin than in other children whose cells have not been previously stimulated by such exposure. This is the case even though these

exposures have been slight and have not been apparent in the form of a perceptible increase of antitoxin in the circulating blood. After a first series of toxin-antitoxin injections, the immunity responses to the second series did not follow the same inverse ratio noted between original susceptibility of the children in a school and the percentage of successfully immunized children in the same school. Three doses of toxin-antitoxin, each from 1 to 1.5 cc, injected at intervals of one week give much better immunity results than two doses of the same amount injected one week apart. A longer interval between the injection of the toxin-antitoxin has the advantage of allowing the local reaction to disappear more completely before the next injection of toxin-antitoxin is given. There may also be a better antitoxin response when the injections are given two weeks apart. At least six months should be allowed to elapse after the injections of toxin-antitoxin before the Schick retest is made to determine accurately the development of an active immunity. A second series of two or three injections of toxin-antitoxin should be given to those who have not become immune after the first series. There are a few children who fail to develop immunity after toxin-antitoxin injection even after they are given several series. In the schools reported, from 70 to 93 per cent of children were rendered immune after two series of toxin-antitoxin injections. There is practically no danger from anaphylaxis either in repeating the injections of toxin-antitoxin or in giving toxin-antitoxin after a preliminary injection of antitoxin.

The Food Requirements of Children: Fat Requirement.—Holt and Fales (*Am. Jour. Dis. Child.*, 1922, **23**, 471) say that many of the functions of fat in the diet are still subjects of debate. A certain amount of fat should be supplied to provide fat-soluble vitamin. This amount is not yet known. It may be exceedingly small, but until this is known it seems wise not to reduce the fat supply greatly lest there may be a deficiency in vitamin A. Fat probable has an important influence on mineral metabolism, especially on calcium metabolism; for the best absorption of calcium they have found it desirable to supply as much as 3 gm. of fat per kilo in the early years and as much as 2 gm. per kilo after six years. Fat is probably necessary for proper digestion and utilization of protein and on this account it seems desirable to supply as much fat as protein in the diet. Fat helps to maintain normal physical, bacteriological, and chemical conditions in the intestine. It also exerts a protective action against the irritating effects of the products of carbohydrate fermentation. A great reduction in fat in the diet increases the susceptibility to infection, especially to tuberculosis. The nursing infant receives a generous amount of fat, usually as much as 4 gm. per kilo daily. The infant taking modifications of cow's milk usually receives about 3.5 gm. per kilo daily. Older children studied by the authors took on an average over 3 gm. per kilo when under six years of age, and about 3 gm. per kilo during the remainder of the growth period. The grounds for the current impression regarding the harmful effects of fat on children should be investigated carefully. There seems to be little evidence that a liberal amount of fat in the diet is harmful to children with normal digestion and much evidence that fat is an important and necessary component of the diet during the

entire growth period. In general, it seems rational to supply in the diet of the child as much as 4 gm. per kilo daily at one year, decreasing to about 3 gm. per kilo at six years, and maintaining this value throughout the remainder of the growth period.

Milk Ingestion in Relation to Changes in Body Weight of Newborn Infants.—ADAIR and STEWART (*Jour. Am. Med. Assn.*, 1922, **78**, 1865) found that the average body weight for 149 first-born and also for 149 later-born infants, whose birth weights ranged between 2500 and 5000 gm., decreased to a minimum on the fourth day, counting the date of birth as the first day. The average loss amounted to approximately 8 per cent of the birth weight for the first-born infants and to approximately 6.4 per cent for the later-born infants. There was no progressively uniform daily decrease in weight; for each group the greatest loss occurred on the second day. Following the fourth day the average body weight for each group progressively increased. On the tenth day, however, the average weight of the first-born and of the later-born was still 2.4 and 2.6 per cent respectively below the initial weight. For each group of babies the greatest daily gain in weight occurred on the fifth day after birth. For the first-born infants of both sexes the amount of breast milk obtained increased rapidly from an average of 13.0 gm. per feeding on the second day to 54.9 gm. on the fifth day. From the sixth to the tenth day inclusive the increase continued, although less rapidly, the average meal on the tenth amounting to 78.4 gm. With the later-born infants of both sexes the average amount of milk per feeding increased from 16.9 gm. on the second day to 59.4 gm. by the fifth day. On the tenth day the food intake averaged 84.7 gm. per feeding. Throughout the period studied the babies of multiparous mothers averaged larger feedings than the babies of primiparous mothers. The heavier infants in general obtained more milk from the breast per feeding than the lighter ones whether first or later born, particularly after lactation was well established. Of each weight group the average meal in general was larger for infants of multiparous mothers than for those of primiparous mothers. Except for the eighth and ninth days, the average amounts of mother's milk taken daily for each kilogram of body weight was slightly higher for later-born than for first-born infants. The average amount of 10 per cent lactose solution taken per feeding increased to a maximum on the second day. On the following three days, as the supply of milk increased, the lactose solution ingested progressively decreased. There was no apparent difference in the amount of lactose solution taken during this period by the later-born as compared to the first-born babies.

Observations on the Heart in Mothers and the Newborn.—SMITH (*Jour. Am. Med. Assn.*, 1922, **79**, 3) found by clinical, cardiographic and radiographic examination that pregnancy in itself does not cause cardiac enlargement. Such evidences of cardiac enlargement as may be present in the expectant mother under certain circumstances of examination are shown to disappear under other circumstances. Cardiac enlargement in the latter half of pregnancy may be simulated by the upward pressure of the gravid uterus upon the heart, causing cardiac displacement. There are no heart affections which are characteristic

of, or incident to, pregnancy. While pregnancy in all likelihood throws a load of some degree on the heart, the heart is fully capable of adjusting itself to this as it is to other physiologic demands. A definite history of previous infections requires that the expectant mother be closely observed as pregnancy advances for symptoms of masked heart disease, which may not become apparent until brought to light by the heart load of pregnancy. Focal infections may cause symptoms of heart embarrassment in pregnant patients which might erroneously be attributed to pregnancy. Definite cardiac indications for the interruption of pregnancy are rare. Even frankly diseased hearts will exhibit a surprising adaptability to the physiologic demands of pregnancy. The right side of the heart is enlarged in the newborn. Evidence of cardiac enlargement persists for five weeks or longer before the baby's record begins to assume adult characteristics. The heart following birth is frequently irregular at intervals during the first week. Such irregularities may be expected to disappear at a later date and are not indicative of cardiac pathology. Graphic records suggest that it may be possible for maternal irregularities to be transmitted to the child. In a stillborn baby evidences of heart activity were observed for three hours and twenty-four minutes following stillbirth. Massage of the heart through the chest wall may prove to be a useful adjunct to other methods of resuscitation of the stillborn.

The Severe Blood Diseases of Childhood.—POYNTON, TURSFIELD and PATERSON (*Brit. Jour. Child. Dis.*, 1922, **19**, 57) in discussing types of severe blood diseases take up a consideration of von Jaksch's anemia or anemia pseudoleukemica infantum. They group four of their cases under this heading. The criteria which they have adopted are that the child should be under four years of age, that the anemia should be severe, that there should be an unusual proportion of myelocytes present in the peripheral blood, and that the spleen should be of considerable size. In addition, though not invariably present, normoblasts and megaloblasts are commonly found in the films of the blood. Judged by these standards three of these four cases undoubtedly belong to the category of von Jaksch's disease, but the remaining one was doubtful. In this patient the hemoglobin was unusually high and the proportion of myelocytes was unusually low, nor had the spleen such a size as is usually associated with the disease. The erythrocyte count was higher than is expected and the improvement was exceptionally rapid. The general appearance of the patient coupled with the appearance in the blood of myelocytes, normoblasts and megaloblasts led them to believe that this was an example either of a comparatively late stage in convalescence from the disease, or possibly an example of unusually mild degree of the affection. They admit that such a case affords some support to the argument of those who believe that von Jaksch's anemia is not a clinical entity, but an unusually severe stage of any infantile anemia, the uncommon features being merely an expression of the severity of the intoxication. Of the three cases two recovered and one died. Postmortem examination showed petechiæ in many organs, an old blood-clot in the pelvis of one kidney, general moderate enlargement of the lymphatic glands and hypertrophy of lymphoid tissue of the body, and a large firm spleen with marked fibrosis.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Chemical Observations on the Toxemias of Pregnancy.—DE WESSELOW, chemical pathologist to St. Thomas Hospital, London, contributes *Jour. Obst. British Empire*, 1922, **29**, a very interesting paper upon this subject. At the present time it is the belief of obstetricians that the toxemia of pregnancy is especially dangerous to the future health of the patient. It is a curious and interesting fact that pregnant patients who have eclampsia and recover are left in better physical condition than are those who recover from toxemia without eclampsia. The excretory organs in eclamptic patients are in better condition than in those who do not have convulsions. Hence at the present time obstetricians are devoting their attention to the detection of toxemia in its early stages, with the hope of inducing labor sufficiently promptly to bring about a perfect recovery in the patient. With these facts in mind the importance of the writer's paper is evident. Space does not permit an extended review of this paper. The writer concludes that chemical study should in future be of definite value in averting the risk of permanent damage to the mother and indicating the stage at which the induction of labor becomes necessary. The definitely raised urea content of the blood above 40 mgm. per 100 cc is proof that the kidney is severely damaged and is an indication for induction of labor. Where the blood urea is not increased, the urea concentration test gives valuable evidence of the condition of the renal function, and when the figure obtained is below 2 per cent, termination of the pregnancy should be considered. It is of the utmost importance that both these examinations be repeated at regular intervals, the frequency depending upon the urgency of the case. If a rising blood urea is present with a falling concentration capacity, this is an obvious indication of a progressive lesion. Where the diastolic blood pressure is low, it is probable that there is chronic disease, and that a less complete recovery must be expected. Blood-pressure observations are valuable in all cases. We have no efficient and reliable method of estimating hepatic function. By the methods just described we can arrive at definite criteria for interrupting pregnancy.

A Sign of Intrauterine Death.—SPALDING (*Surg., Gynec., and Obst.*, June, 1922, p. 754) calls attention to the value of roentgen-ray pictures where during pregnancy there is fear of intrauterine fetal death. For a basis of study 27 patients in normal pregnancy were examined by the roentgen-ray. The outline of the fetal skull was distinct in each case; there was no overlapping of the bones, nor did there seem to be any shrinkage from a normal size. One patient who had a normal pregnancy had rupture of the membranes in the beginning of labor; she had a long first stage (forty-three hours) because of rigidity of the cervix, but she was

finally delivered of a living child. A roentgen-ray picture taken late in the first stage of labor showed marked overlapping of the fetal bone but no sign of diminution in the contents of the skull. The absence of diminution in the contents of the cranium showed that the condition was the result of pressure and not of fetal death. In three cases of intrauterine death the roentgen-ray picture showed marked overlapping of the skull bones with distinct signs of shrinkage in the contents of the skull.

Labor Complicated by Infected Fibroid.—HOLLAND (*Jour., of Obst. British Empire*, 1922, **29**,) describes the case of a multipara, aged thirty-five, who had been delivered three weeks previously, her child weighing six and a half pounds, and living but one day. The uterus remained large, the placenta did not come away and it was thought that a second child was present. At the end of three days, as nothing had happened, the attending physician removed the placenta by the hand and then made the diagnosis of uterine fibroid. A violent septic infection developed, and when the patient was brought to the hospital she had signs and symptoms of general peritonitis. The uterus was at once removed by supravaginal hysterectomy. On the anterior surface of the tumor there were two perforations, from which pus was oozing. The patient died thirty-six hours after operation. On examining the specimen the muscular capsule of the tumor was very thin. The perforations had occurred through this muscular capsule, and underneath the fibroid was sloughy and yellow in color. These perforations permitted the infective discharge from the uterus to gain access to the peritoneal cavity and set up peritonitis.

Induction of Labor with Castor Oil and Quinine.—WILLIAMSON (*Surg., Gynec., and Obst.*, June, 1922, p. 812) gives his results in induction of labor by the use of castor-oil and quinine in 300 cases. His study was suggested by two cases where these substances produced abortion. One was a primipara three months pregnant, who in six hours took 60 grains of quinine sulphate. She had marked signs of the action of the quinine, and had great pain at the time of abortion, but seemed to have recovered from the drug by the third day. The second patient was a multipara four months pregnant, who took an ounce and a half of castor oil and four grains of quinine. She had sharp pain with profuse vaginal bleeding, which suggested a premature separation of the placenta. In the cases studied, the patient was given a light dinner and in primiparæ castor oil was given at midnight, in multipara at six or seven in the morning. One ounce and a half of castor oil was administered with orange juice or some other vehicle. So soon as the oil was effective an enema at 106°F. was administered, and immediately after this 5 grains of quinine was given and repeated at thirty-minute intervals until 20 grains had been taken. If the patient complained of ringing in the ears or nausea the quinine was stopped. The administration of a grain of pepsin with the quinine prevented nausea. Occasionally two doses of 10 grains were given two hours apart. The aid seemed to play no part in the occurrence of labor. If the attempt failed, the second trial was not made until ten days later. Of the 300 cases the method was successful in 140, unsuccessful in 160. In those where labor did not come on, all the primiparæ were at full term except

20, and the head of the fetus had engaged in all but 8. The reason for attempting induction was moderately contracted pelvis or an impending toxemia. All the multiparæ were due at date excepting 28. In 20 of these patients the head had not engaged; induction was attempted because of toxemia or because the patient was going over time. The writer believes that this method is successful in about half of the cases. With these patients labor should be carefully watched, for occasionally the uterus contracts violently. If mother or child seems to be in distress the obstetrician should interfere at once. Quinine should be stopped as soon as there is evidence of cinchonism. This method is apt to be most successful when the patient is at full term or a little past, when the head is engaged in the pelvic brim and when the uterus is irritable. The mechanism of labor induced in this manner results from irritation by the castor oil on the sympathetic centers with increased peristalsis; and increase of the rhythm and muscle tone produced by the quinine acting directly on the uterine muscle.

Rupture of the Uterus through a Cesarean Scar.—GRAHAM (*Jour. Obst., British Empire,* 1922 **29,**) reports the case of an elderly primipara on whom he had performed a Cesarean section. A little more than a year later a pregnancy occurred and the induction of premature labor was attempted by the insertion of bougies. The pelvic contraction was not excessive, and it was hoped that vaginal delivery could be affected. As pains had not developed this treatment was abandoned, a Cesarean section performed, securing a living child. On this occasion the uterus was closed by two layers of continuous iodine-catgut sutures, and uninterrupted recovery followed. Two years later another pregnancy occurred and the advice was given to have Cesarean section with sterilization of the patient, as her general health was not good. Six weeks before term the patient was brought to hospital because of severe abdominal pain and profuse bleeding from the vagina. No fetal heart sounds were heard, but the child was unusually mobile. On opening the abdomen the uterus was found ruptured with the fetus and placenta free in the abdominal cavity. The patient recovered with hysterectomy. On examining the muscle of the uterus there was a general fibrosis. At the site of the last incision healing had been imperfect in the deeper two-thirds of the scar. The granulation tissue was cellular, vascular, and imperfectly organized. The epithelium of the endometrium had grown into the scar, showing that union had never occurred in the deeper tissues.

Twin Pregnancy and the Diagnosis of Superfetation.—CALDERINI (*Annali di Ostetricia,* January, 1922, p. 1) has studied a case of twin pregnancy and the possibility of diagnosing superfetation. He investigated the centers of ossification and also the placenta, which was one large placenta with two cords, and the two amniotic sacs divided by a partition. The paper has several good illustrations, showing the structure of the placenta and roentgen-ray examination of the skeleton. He finds that a positive statement regarding superfetation is difficult to make. All of the factors in the case must be thoroughly studied, and he believes that all data should be collected by clinics, so that they can be compared in the reporting of various cases. Evidently

greater study is required in the physiology of fecundation, before a positive diagnosis of superfetation can be made. (In this connection the reader's attention may be called to a recent paper by RADASCH, *Surg., Gynec. and Obst.*, April 1, 1921, p. 339.)

Blood-pressure in Pregnancy.—Normal blood-pressure of pregnant women has been studied by LITZENBURG, (*International Clinics*, 1921, **4**). His series of cases numbered 524. Illustrative cases are cited, and the writer concludes that the normal systolic blood-pressure in pregnant women is from 100 to 130 mm., and not from 100 to 150 mm. as quoted by various writers. The normal diastolic pressure is from 60 to 85; and the normal pulse pressure from 30 to 50. Pressure above these averages indicates a pathological condition and demands close observation of the patient. In 30 per cent of these cases there was an increase of blood-pressure during pregnancy, and in 21 per cent a decrease; while low blood-pressure does not indicate that shock is inevitable, it points to a depressed condition of the woman's general health. One pregnant woman in ten had a systolic pressure above 130 and required special attention. In studying the toxemia of pregnancy an increase in blood-pressure is our most valuable sign. Albuminuria is also of great importance, but a high blood-pressure is present earlier than albuminuria. Where the tension increases, it forms a system of great value. All pregnant women whose systolic blood-pressure was above 180 were found to be definitely toxemic. When blood-pressure was above 160, 50 per cent were markedly toxemic; and when between 150 and 160, 35 per cent; when between 130 and 140, 3.5 per cent of patients were markedly toxemic. Other diseases than toxemia and some unknown conditions may cause high tension. The danger of convulsions increases steadily with systolic tension above 160 mm.; convulsions, however, may occur with moderate or low blood-pressure. Eclampsia in most cases can be prevented if pregnant patients are early and frequently examined, and in this examination the study of blood-pressure is of very great importance. This and the examination of the urine is our surest method of diagnosing toxemia.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

INSTRUCTOR IN GYNECOLOGY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Elephantiasis Vulvæ.—In discoursing upon elephantiasis of the vulva, or, as he prefers to call it, the hypertrophic-ulcerative form of

chronic vulvitis, TAUSSIG (*Amer. Jour. Obst. and Gynec.*, 1922, **3**, 281) states that he believes that there is a distinct racial predisposition to this disease. When we consider that the negro makes up but one-tenth of the population of this country, it is striking that practically all of the cases of vulvar hypertrophy in the American literature are found among colored women. It is probable that this tendency to fibrous hypertrophies of the vulva among colored women has some relationship to the similar tendency to keloids and uterine fibroids in this race. Another factor to be considered in this disease is that the anatomic distribution of the lymph-channels of the vulva predispose to lymph stasis. In filarial infections the occurrence of a lymphatic enlargement in the inguinal and femoral region not only blocks the flow to the leg but also to the labium on the same side. Lymph stasis of some degree, whether in the groin or in the labia, must be considered as a *sine qua non* in the production of these enlargements. The looseness of the vulva skin makes possible the formation of chronic edematous deposits, with resulting fibrosis and enlargements of these parts. Together with the eyelids and the backs of the hands, the vulva is one of the first points at which a tendency to edema will be manifested. Uncleanliness is another important etiologic factor, as in no instance has this disease been found among women of the better classes. Persons with neglected syphilis and gross lesions about the external genitals may develop a slight thickening of the tissues, but if they are clean about their person they do not develop these extreme hypertrophic ulcerations. Often a syphilitic rectovaginal fistula, together with a gonorrhea, makes it difficult to keep the parts clean. On the other hand, once the condition has developed, the best care and hospital nursing, trying to keep the parts clean, will not materially influence the size of the mass or the extent of the ulcerations. The disease is found solely during the period of greatest sexual activity, and it is certain that the repeated traumatisms of coitus, especially in prostitutes, has much to do with the production of hypertrophy. The frequent occurrence of tertiary syphilitic ulceration about the vestibular ring results in repeated injuries with resulting wound infection following coitus. The poor nutrition of these parts produced by the lymph stasis and obliterative endarteritis make wound healing slow, so that in most instances these ulcers do not heal entirely and must be excised. As to the nature of the infecting agent in this disease, there is much difference of opinion. Syphilis is found in from 80 to 90 per cent of the patients, but there is some difference of opinion as to whether the lesion is to be classified as a tertiary gummatous deposit or as a postsyphilitic process, since many of these cases have a negative Wassermann reaction with positive evidence of a previous syphilis. While text-books on gynecology have in the past emphasized filariasis as a factor, it is apparently rather rare. Tuberculosis of the vulva has been found in some few cases associated with these hypertrophic tumors. Gonorrhea is probably never a primary factor, but will often greatly increase vulvar irritation and so, secondarily, aids in the growth of the vulvar enlargements. Symptoms are usually insignificant in this disease, which may be due to the low state of intelligence and lowered pain sense in these individuals. Some discomfort from the weight of the pendulous mass, interference with

walking, and urinary and rectal irritability may be noted. A word may be added regarding the treatment of these cases. Antisyphilitic treatment, even the most persistent and vigorous, will not cure these cases and will only rarely and temporarily affect the size of the tumor mass. It is well, however, that such treatment be employed to promote prompt healing after surgical intervention. The record of the seven cases that underwent operation in Taussig's series shows the uniformly satisfactory results of vulvectomy in these cases, provided only that the incision be wide enough to include all indurated and ulcerated tissue and it is usually better to make this incision with the cautery.

Action of Emetin Hydrochloride upon the Uterus.—In Central Africa a few years ago MARTIN (*Amer. Jour. Obst. and Gynec.*, 1922, **3**, 241) treated a white woman, in the sixth month of pregnancy, suffering from a dysenteriform enteritis (without amebæ in the stools). Not responding to ordinary treatment, she was given for three consecutive days one hypodermic injection of one grain of emetin hydrochloride. The drug had no action upon the enteritis and on the morning following the last injection the patient went into labor and aborted the same evening. This suggested to Martin to test the action of this drug upon the uterus, which he did by means of experiments upon laboratory animals. The most important finding in this work was that the action of emetin upon the uterus differed *in vitro* and *in vivo*. *In vitro* emetin lessens the activity of pregnant and nonpregnant uterus (dogs, rats, rabbits). It causes a decrease in tone and amplitude, although increasing the rate of contractions. *In vivo* emetin causes an increase in the tone of the uterus, both pregnant and nonpregnant (dogs and rabbits). Therefore it might be tested with caution in the treatment of metrorrhagia and menorrhagia, owing to the fact that it increases the tone of the uterus *in vivo*.

Radium Treatment of Benign Bleeding.—In presenting his opinions concerning the use of radium in hemorrhage from the uterus of benign origin, POLAK (*Med. Rec.*, 1922, **101**, 493) first considers myopathic hemorrhages in young girls, which are frequently excessive, although they sometimes yield to the internal administration of endocrines and regulation of the lower bowel. When the bleeding has continued for any length of time the endometrium becomes hypertrophied, the uterus large and soft and the os is very likely to be open. These cases were formerly curetted after all other forms of internal medication had failed and a secondary anemia had been induced. After curetting there was usually an amenorrhea for a month or two, when this was followed by a metrorrhagia. This same case treated by radium for from 300 to 600 mgm. hours, with the radium properly filtered, will establish a normal menstruation after one seance. He has treated 31 such cases and in only 1 case was it necessary to repeat the exposure. Six of these girls are now married and two have become pregnant, a fact which answers some of the criticisms which are made of using radium in young girls. In regard to myomata, radium will control the hemorrhage from uterine myomata and in a large number of cases will reduce the size of the tumor, provided the tumor is intramural or submucous

and not pedunculated. Nevertheless operation is still the procedure of choice in most myomata, for the indications for radium are limited and it has certain definite disadvantages, such as: First, while it controls bleeding and the majority of cases show a reduction in the size of the tumor, nodules outside of the uterus may be left without a blood supply and consequently are more likely to give trouble. Second, malignant complications already in the tumor may be overlooked, for it has been shown that sarcoma is found in serial sections in about 9 per cent in submucous tumors; consequently we can lay down the dictum that radium is never permissible in submucous growths or unless a diagnostic curettage is possible, for while remarkable results have been shown following radiation of cervical cancer, body carcinoma is not amenable to the effects of the rays. Third, about 54 per cent of all fibroids are complicated by some form of tubo-ovarian disease; consequently many of these intrapelvic complicating lesions are missed, and while the tumor is shrunk and the hemorrhage controlled the associated lesions help to keep up the patient's invalidism. Fourth, radiation, when applied in sufficient dosage to check hemorrhage and shrink the tumor, will seriously impair the reproductive functions in young women, and therefore should not be used as a procedure of choice in this class of cases. Fifth, one of the symptoms of fibroids which requires treatment is the pressure symptom; here the effect of radium is too slow to relieve the condition which intraligamentous growths produce on the ureters and bloodvessels. Sixth, the immediate effect of radium is the production of edema and excitation of inflammatory reactions; hence, in the presence of old inflammatory adnexal lesions, this reaction becomes more marked. Finally, radiation will increase the necrosis in tumors which are already necrotic, and by added acidosis increase the toxemia of the patient. Against these disadvantages radium has certain definite advantages in treatment of fibroid tumors, particularly if the proper selection is made. These advantages are: First, there is no operative mortality, there is no general anesthetic, there are no postoperative complications, and there is prompt control of uterine hemorrhage. Second, should radium fail, operation is always possible. Third, the menopausal symptoms are not so marked. Fourth, in intramural tumors we cannot only expect absolute cessation of the hemorrhage, but shrinking in the tumor in over 65 per cent of the growths. Fifth, radium is the procedure of choice in myomata complicated by heart disease, extreme anemia, diabetes, and chronic nephritis. Of the 106 growths which Polak has radiated only 2 have needed subsequent operation. In 80 of the tumors the growth shrunk to less than half of the original size and in 20 cases it has entirely disappeared.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

DIRECTOR OF THE PATHOLOGICAL LABORATORIES, SAO PAULO, BRAZIL,

AND

DE WAYNE G. RICHEY, B.S., M.D.,

ASSISTANT PROFESSOR OF PATHOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

The Action of Neoarsphenamine and Neosalvarsan on the Phagocytic Activity of Leukocytes.—To test the action of arsenical compounds on phagocytosis, TUNNICLIFF (*Jour. Infect. Dis.*, 1922, **30,** 545) mixed equal parts of neoarphenamine in salt solution, normal human serum, suspensions of washed human leukocytes and of strains of Streptococcus viridans not spontaneously phagocytable which were incubated for twenty-five minutes. Salt solution alone was used in the controls. The mixtures were smeared on slides, stained with carbol thionin and at least 100 polymorphonuclear leukocytes were counted. To determine whether the effects on the degree of phagocytosis were on the leukocytes themselves, equal numbers of washed leukocytes were suspended in different dilutions of the arsenical compound for one hour at room temperature. The leukocytes were washed twice in salt solution and equal quantities of serum and bacteria added, incubated for twenty-five minutes and smears made as before. It was found that solutions of neoarsphenamine below 1 to 1000 stopped or greatly reduced phagocytosis, while dilutions between 1 to 10,000 and 1 to 100,000 increased phagocytosis on an average more than twice. Five of seven rabbits each injected with 0.007 gm. of neoarsphenamine showed a decided increase in the number of leukocytes in from fifteen to thirty minutes following the administration and the leukocytes were from 2 to 6 times more actively phagocytic than normal at fifteen minutes after inoculation of the arsenic compound. No changes in the opsonic index were observed. Two patients showed no leukocytosis after injection, but in thirty minutes subsequent to inoculation there was an increased phagocytic activity of the leukocytes. This activity disappeared fifteen minutes later. Similar results were obtained with neosalvarsan. For reasons stated in the context, the author believes that the arsenic compounds were directly responsible for the increased phagocytic activity.

Studies on the Nature of the Action of Nonspecific Protein in Disease Processes. III. Nonspecific Proteins and Soluble Toxin.—Having demonstrated before that 1 cc of normal horse serum when injected subcutaneously into guinea-pigs will protect against a fatal dose of diphtheria toxin and may protect against as high as eight fatal doses and that the protein of normal horse serum (precipitated by alcohol) will also protect against diphtheria toxin, COWIE and GREENTHAL (*Jour. Med. Research*, 1922, **43,** 21) continued their experiments

to ascertain whether this protecting action is due to the protein or to native antitoxin. It was learned that the protective action of normal horse serum precipitated by alcohol is much less than that of untreated horse serum; that the globulin (alcohol treated) fraction of horse serum protein is more effective than the albumin fraction similarly treated; that the nonalcohol treated globulin fraction of 1 cc of normal horse serum will protect against several fatal doses of diphtheria antitoxin, while the alcohol-free albumin fraction furnishes no protection; that no protective action against diphtheria toxin was observed when egg white, milk and guinea-pig and rabbit serum were used, and that 1 cc of normal horse serum when injected subcutaneously into a guinea-pig will protect against a fatal dose of tetanus toxin. From this evidence the authors believe that the protective action of normal horse serum against soluble toxin is due to natural antitoxin in the serum and not to the effect of the nonspecific protein.

An Experimental Study of the Effects of Protein Injections upon Infections.—In view of the results which have been reported relative to the favorable influence of protein injections upon various infections and the practical absence of unfavorable comment, KROSS (*Jour. Med. Research*, 1922, **43**, 29) conducted three series of experiments in order to test the effect of protein therapy upon certain infective processes in animals. Accordingly, white rats were inoculated with mouse typhoid bacilli, a general peritonitis was produced in rats, rabbits and guinea-pigs by soiling the peritoneum with their own gastric or intestinal contents and rabbits were injected intratracheally with a virulent broth culture of Pneumococcus I. The protein was administered by subcutaneous, intraperitoneal and intracardial methods in different groups and consisted of 1 cc of a 1 per cent solution of nucleinic acid. It was found that the protein did not increase the resistance of the animals to any of the infections experimentally produced. The treated animals could not overcome the infection any better than the untreated ones. Moreover, the protein inoculation seemed to reduce the vitality of the animals and the danger of death from anaphylactic shock was "such as to stamp this method of treatment as actually threatening great potential harm."

Frequency of Bacillus Influenza in the Nose and Throat in Acute Lobar Pneumonia.—STILLMAN (*Jour. Exper. Med.*, 1922, **35**, 7) reports the incidence of Bacillus influenzæ and pneumococcus in the noses and throats of patients with acute lobar pneumonia and refers to the frequency of the former organism in cultures recovered from normal individuals. The throat cultures were obtained by passing cotton swabs over the posterior pharyngeal wall and the nasal cultures by passing cotton swabs through a sterile speculum into the nares. The swabs were inoculated on freshly poured oleate hemoglobin plates and on fresh blood-agar plates. In 31 cases of pneumonia 18 (58 per cent) showed influenza bacilli in the throat and from 35 pneumonia patients, the same organism was isolated from the nose on 9 occasions (23 per cent). In certain other cases, influenza bacilli were encountered in the sputum when they were not found in the nasal or pharyngeal cultures, so that among the entire 35 cases, influenza bacilli were isolated from at

least one of these three sources in 30 or 85 per cent of cases. Of 1077 normal individuals Bacillis influenzæ was found in the throats in 30 per cent. Whereas pneumococci were rarely encountered in the nose cultures of normal persons, they were demonstrated in 15 of the 35 cases of lobar pneumonia, the majority of which were found to be the same type as the organisms in the lung lesions as shown by sputum determination. The influenza bacilli encountered in this work were of various types. The author states that the exact significance of these findings is at the present time not clear.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Carbon Tetrachloride: A Drug Proposed for the Removal of Hookworms, With Special Reference to its Toxicity for Monkeys when Given by Stomach Tube in Repeated Doses.—LAKE (*Public Health Reports*, 1922, **37**, 1123) reports on experiments on monkeys designed to determine the effect of carbon tetrachloride which is coming into use as a treatment for hookworm infestation. The results are summarized as follows: (1) Four monkeys received carbon tetrachloride by stomach tube in amounts of 1, 2, 3, and 5 cc respectively, at intervals of two to three days, over a period of from thirty to forty-one days, the total number of doses varying from 12 to 16. (2) No symptoms of importance were shown by the monkeys during this period. (3) The two monkeys receiving the larger doses were subsequently used for the testing of suspected poliomyelitis virus and died of brain abscess. In each case gross and microscopic examination of the important organs failed to show any changes indicative of an exogenous poisoning. (4) The doses received by the monkeys at each treatment were from 10 to 40 times greater in cubic centimeters per kilogram of body weight than the dose mentioned by Hall as that indicated for man, and these doses were repeated from 12 to 16 times. From the data at hand we must conclude that carbon tetrachloride by stomach has a very low toxicity for monkeys and that it is probable that man may safely be given considerably higher doses than the ones suggested by Hall, and that it might be safe to repeat the dosage several times at proper intervals (one week). Finally, in view of the unusually promising results that carbon tetrachloride has given as an anthelmintic for hookworms in

animals, and in view of its unusually low toxicity for animals, including monkeys, when given by stomach, both in single and in repeated doses, we believe that it deserves an extensive trial in the treatment of hookworm diseases in man.

A Rapid Method of Determining the Presence and Type of Botulinus Toxin in Contaminated Foods.—Realizing the importance of an early diagnosis of botulism, ORR (*Jour. Infect. Dis.*, 1921, **29**, 287) has utilized white mice, some of which have been injected previously with Type A antitoxin and some with Type B antitoxin in arriving at the knowledge of both the presence and type of botulinus toxin in contaminated foods. About 0.5 cc of the filtrate of the infected food was introduced intraperitoneally into normal mice and mice protected by the Types A and B antitoxin. If previously immunized mice are not available, it is efficient to mix some of the suspected toxic filtrate with Type A antitoxin and some with Type B antitoxin and then inject the mixture into mice. As the specificity of the toxin and antitoxin of the two types, A and B, is very distinct, if the food contains the toxin of Bacillus botulinus A, the mice receiving no antitoxin and those receiving Type B, antitoxin will die, while those receiving Type A antitoxin will survive. On the other hand, if the food contains toxin of the Type B organism, only those receiving Type B antiserum will live. In this way both the presence and the type of toxin may be determined in from four to six hours. As the toxin may be present in weak concentration, it is advisable to inoculate some mice with larger quantities of the suspected filtrate.

Smallpox in Twenty States.—FORCE and LEAKE (*Public Health Reports*, 1921, **36**, 1979) make an analysis of state laws and regulations bearing on smallpox vaccination, and compare the results with the rates in the states under consideration. Their conclusions are as follows: "From a study of these statistics and procedures it is evident that smallpox in this country is dependent on the popular vote. In general the people obey laws which they have made. If popular sentiment in a state is behind a strong centralized compulsory vaccination act, smallpox is negligible in that state. If local authorities are given discretionary powers in the matter of vaccination enforcement the rate tends to rise, even in the most favored sections of the country, whereas in the absence of compulsory features of the law, or where there is no law at all, smallpox reaches a high rate."

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this* JOURNAL.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

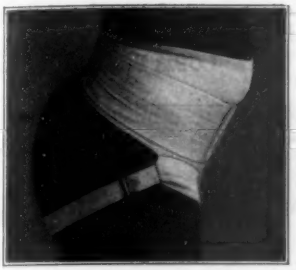
DR. JOHN H. MUSSER, JR., 262 S. 21st Street, Philadelphia, Pa., U. S. A.

Trade Mark **STORM** Trade Mark

Binder and Abdominal Supporter

(Patented)

Trade Mark



Trade Mark

For Men, Women and Children

For Ptosis, Hernia, Pregnancy, Obesity, Relaxed Sacro-iliac Articulations, Floating Kidney, High and Low Operations, etc.

Ask for 36-page Illustrated Folder
Mail orders filled at Philadelphia only—within 24 hours

Katherine L. Storm, M.D.

Originator, Patentee, Owner and Maker

1701 DIAMOND ST. PHILADELPHIA

FOR INFANTS

Nursing Mothers Invalids and Convalescents

The Original

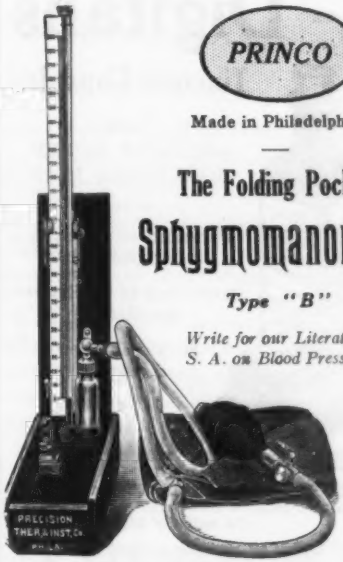
A COMPLETE FOOD

Safe Uniform Reliable

Endorsed by the medical profession for over 1/3 century

AVOID IMITATIONS

1910 **1922**



PRINCO

Made in Philadelphia

The Folding Pocket

Sphygmomanometer

Type "B"

Write for our Literature S. A. on Blood Pressure

Precision Thermometer and Instrument Co.

1434 Brandywine Street - Philadelphia, Pa.

In Bronchitis *and* Tuberculosis

Calcreose is particularly suitable as an adjunct to other remedial measures.

Calcreose contains in loose chemical combination approximately equal parts of creosote and lime.

Calcreose has all the pharmacological activity of creosote but does not cause any untoward effect on the gastro-intestinal tract, therefore Calcreose may be taken in comparatively large doses for long periods of time.

Sample on request.

The Maltbie Chemical Co.

Newark, New Jersey.

CALCREOSE

"Upsher Smith" Brand

Digitalis

Tincture-Capsules

From
AMERICAN GROWN
MINNESOTA LEAF

Prescribed exclusively by leading cardiologists

Standardized by the Hatcher-Cat Method

For You and Your Hospital

IN TWO FORMS ONLY:—

CAPSULES FOLIA-DIGITALIS (Upsher Smith). Each contains 1 grain or 1 cat unit of the standard leaf. *In bottles of* 24, 500 *and* 1000

TINCTURE DIGITALIS (Upsher Smith). U. S. P. process, 10 minims representing one grain of our standardized leaf or one cat unit. *In* 1 *oz. bottles*

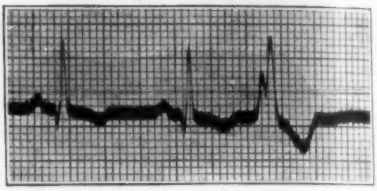
Tell your druggist and hospital you want Upsher Smith's Digitalis products. Write for literature, direct from grower

UPSHER SMITH, Inc., 720 Washington Ave., S.E., Minneapolis

"Electrocardiography

is the last court of appeal and its judgment is rarely at fault."

LOUIS F. BISHOP, M.D.



Electrocardiogram showing normal complex with ventricular extrasystoli

Practitioners, clinics and hospitals find it essential for a complete examination, and the returns capable of creating its own maintenance fund besides allowing a generous surplus each year.

Catalog and Details on request

Charles F. Hindle & Co.
OSSINING-ON-HUDSON NEW YORK

HÆMATIC OPOTHERAPY

used by the Paris Hospitals prescribed by over 30.000 Physicians

REPLACES

RAW MEAT AND IRON

DESCHIENS' SYRUP

In each tablespoonful there are 40 grains of active Hæmoglobin, an equivalent of a fifth-of-a grain of vitalized iron. One tablespoonful at the beginning or at the end of the two principal meals of the day. In cases of serious anæmia, double the dose.

Made in France in
LABORATOIRES DESCHIENS
9, rue Paul-Baudry, PARIS

Samples on application to
G. J. WALLAU INC
6, Cliff S', NEW-YORK

MANY CHRONIC CASES REQUIRE INSTITUTIONAL CARE

THE advantages of institutional treatment for stomach and intestinal disorders, Neurasthenia, Heart Disease, Diabetes, Obesity, Nephritis, Rheumatism and other stubborn chronic maladies are worthy of consideration.

A most important advantage is the isolation of the patient from harmful influences, substituting conditions and surroundings that are altogether recuperative for the necessary period of time, is greatly to the advantage of the attending physician.

At Battle Creek, every case receives, first of all, a careful examination. Each patient is submitted to the X-ray and all other up-to-date methods of investigation, including chemical and serological examinations of the blood, efficiency tests of the liver, kidneys and other vital organs, tests for acidosis, metabolism tests and other special tests and researches which may be required to throw light upon the individual case.

For literature or further information concerning the Institution and its methods address

THE BATTLE CREEK SANITARIUM

BATTLE CREEK Box 247 MICHIGAN

IN ACIDOSIS

All the bases of the body are drawn upon (not only sodium) and lost from the body. When only sodium bicarbonate is given the loss of the other bases is not made up.

The use of KALAK WATER makes possible the administration of the several bases in agreeble form—an important matter when patients must take alkalies for longer periods.

Each bottle carries in sparkling form several grammes of the bicarbonates of sodium, potassium, calcium and magnesium.

Kalak Water Company of N.Y.

23 City Hall Place New York City

SALOPHEN

Antirheumatic ***Antipyretic***
Analgesic ***Antiseptic***

For many years Salophen has met the requirements of a safe and agreeable salicyl derivative, no deleterious effects having been observed from its use.

These advantages, together with its tastelessness, render it especially adapted for children and delicate persons.

Particularly good results have been reported from its use in

Colds **Influenza**
Rheumatism **Neuralgias**

How Supplied: Powder, 1 oz. cartons
Tablets, 5 gr., bottles of 25 and 100

Literature on Request

WINTHROP CHEMICAL COMPANY, Inc.
16-22 Hudson Street, New York, N. Y.

MEDICINE

A NEW PERIODICAL

Publishing Analytical Reviews of General Medicine, Neurology, Pediatrics

Edited by David L. Edsall, Harvard Medical School.
John Howland, Johns Hopkins Medical School.
Associate Editor, Paul D. White, Massachusetts General Hospital.

PUBLISHED QUARTERLY. *500 PAGES TO THE VOLUME*

MEDICINE will interest:

1. TEACHERS, who wish to keep in touch with the methods and results of medical work in their own and other fields.
2. CLINICIANS, who wish the advantage of having immediately available, in convenient and readable form, critical digests of the recent views on general medicine, neurology and pediatrics.
3. LABORATORY WORKERS, who require a useful reference work that will give systematic and careful presentations of subjects of important medical interest.

SUBSCRIPTION PRICE, NET POSTPAID

$5.00, United States, Mexico, Cuba **$5.25, Canada** **$5.50, other countries**

WILLIAMS AND WILKINS COMPANY

Publishers of Scientific Periodicals and Books

BALTIMORE, U. S. A.

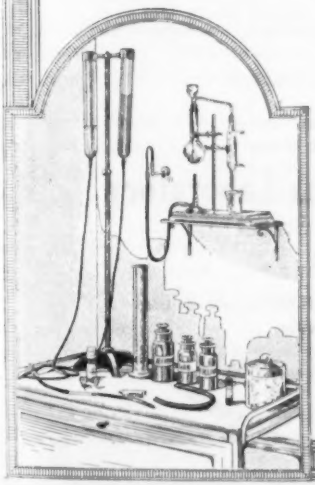
Neosalvarsan

TRADE MARK REG. U.S. PAT. OFF.

(NEOARSPHENAMINE-METZ)

is unsurpassed in reliability, trypanocidal efficiency and ease of administration.

Neosalvarsan is manufactured by the process used in preparing the original Ehrlich product and offers the physician the ideal means for treating the luetic.



HA
M E
T Z
LAB
Trade Mark
Reg. U.S. Pat. Off.

Literature can be obtained from

HA-METZ LABORATORIES, Inc.
One-Twenty-Two Hudson Street, New York.

LOESER'S INTRAVENOUS SOLUTIONS

ACCEPTED BY THE COUNCIL

LOESER'S INTRAVENOUS SOLUTION OF MERCURY OXYCYANIDE, 8 Mgs.

A sterile, table solution in nonsoluble glass ampoules, 5cc containing 8 mgs. (1/8 grain) of Mercury Oxycyanide.

LOESER'S INTRAVENOUS SOLUTION OF MERCURY OXYCYANIDE, 12 Mgs.

A sterile, stable solution in nonsoluble glass ampoules, 5cc containg 12 mgs. (1/6 grain) of Mercury Oxycyanide.

We offer these solutions to the medical profession as a means of carrying on intensive mercurial treatment of syphilis.

The objections to the intramuscular method, lack of uniform absorption, irritation, induration and abscesses, are overcome by the intravenous administration,

The superiority of these solutions of Mercury Oxycyanide over the intravenous administration of the so-called acid salts of mercury, bichloride, biniodide, etc., is due to the fact that they are less apt to cause irritation of the veins, a common fault of most soluble mercury compounds.

Clinical Reports, Reprints, Price List
and
"The Journal of Intravenous Therapy"
Sent to any physician on request

New York Intravenous Laboratory
100 West 21st Street
New York, N. Y.

Producing ethical intravenous solutions for the medical profession exclusively

REDUCED PRICES

NEODIARSENOL (Neoarsphenamine)				DIARSENOL (Arsphenamine)				SODIUM DIARSENOL (Sodium Arsphenamine)			
0.9	Grm.	Amp.	**$1.00**	0.6	Grm.	Amp.	**$1.00**	0.9	Grm.	Amp.	**$1.00**
0.75	"	"	**.90**	0.5	"	"	**.90**	0.75	"	"	**.90**
0.6	"	"	**.80**	0.4	"	"	**.80**	0.6	"	"	**.80**
0.45	"	"	**.70**	0.3	"	"	**.70**	0.45	"	"	**.70**
0.3	"	"	**.60**	0.2	"	"	**.60**	0.3	"	"	**.60**
0.15	"	"	**.50**	0.1	"	"	**.50**	0.15	"	"	**.50**
1.5	"	"	**1.50**	1.0	"	"	**1.50**				
3.0	"	"	**2.75**	2.0	"	"	**2.75**				
4.5	"	"	**4.00**	3.0	"	"	**4.00**				

Orders for 50 ampoules—10% discount

Discount on larger quantities on request

It is with pleasure that we advise you that from this date a very substantial reduction in the prices of Diarsenol, Neodiarsenol and Sodium Diarsenol is made. They will now be supplied at approximately ONE HALF the amount you have been paying for arsenicals of any brand in the past.

This reduction is made possible through the perfection of manufacturing processes which ensure very uniform dependable products, without any losses due to material failing to meet the standards of the United States Public Health Service.

Diarsenol brand products are now unexcelled for solubility, stability, low toxicity and therapeutic power. All are tested at standards very much higher than Government requirements. Each lot is officially tested and passed by the U. S. P. H. S. before being shipped, as all material is made under regulation and control of the Government.

If you are not at present using our arsenicals, try a small order—your dealer can supply it—or a line to any of the offices below will have prompt and careful attention. Literature on comparative therapeutic efficiency mailed on request.

DIARSENOL COMPANY, Inc.

ATLANTA, GA.
Forsyth Bldg.

BUFFALO, N.Y.
Ellicott Square

BOSTON, MASS.
53 State Street

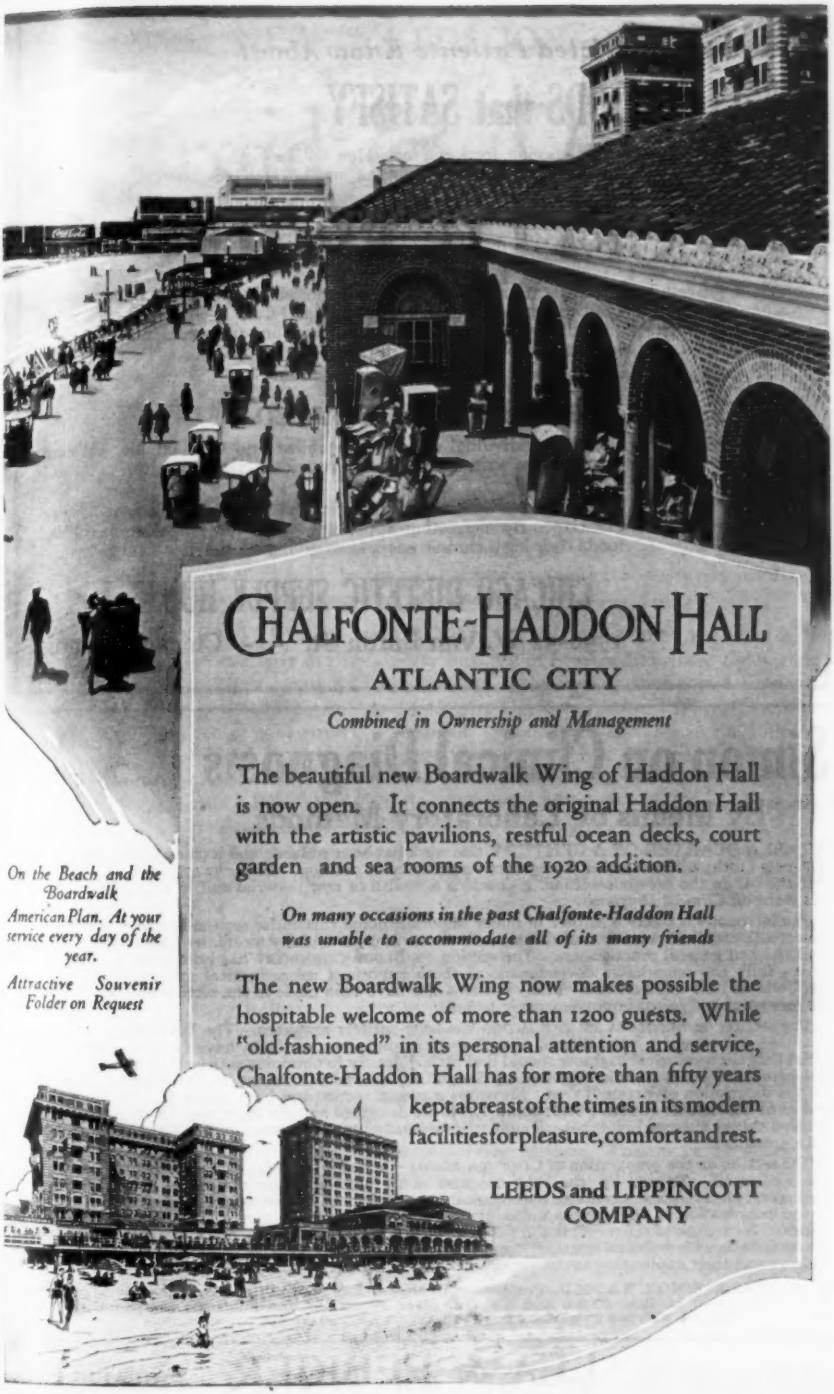
What Is It Worth To Be *Sure?*

TO the physician treating a case of diphtheria or immunizing a child prophylactically, what is it worth to be sure that the Antitoxin or Toxin-Antitoxin used is absolutely dependable? What is it worth to know that he is fighting the disease with products both safe and potent?

The efficacy of Antitoxin and Toxin-Antitoxin in the control of diphtheria has been definitely established. The dependability of these products is predicated on that of the laboratory which makes them. Equipment, personnel, supervision—all of these must be of a high order to insure a trustworthy product. But above all the laboratory supplying these vitally important immunizing agents must be dominated by ideals of service and must be deeply conscious of its responsibility.

"DIPHTHERIA IMMUNIZATION," a reprint, sent on request. Write nearest branch: Detroit, New York, Chicago, Kansas City, Baltimore, New Orleans, St. Louis, Minneapolis, or Seattle.

Parke, Davis & Company



CHALFONTE-HADDON HALL

ATLANTIC CITY

Combined in Ownership and Management

The beautiful new Boardwalk Wing of Haddon Hall is now open. It connects the original Haddon Hall with the artistic pavilions, restful ocean decks, court garden and sea rooms of the 1920 addition.

On many occasions in the past Chalfonte-Haddon Hall was unable to accommodate all of its many friends

The new Boardwalk Wing now makes possible the hospitable welcome of more than 1200 guests. While "old-fashioned" in its personal attention and service, Chalfonte-Haddon Hall has for more than fifty years kept abreast of the times in its modern facilities for pleasure, comfort and rest.

LEEDS and LIPPINCOTT COMPANY

On the Beach and the Boardwalk

American Plan. At your service every day of the year.

Attractive Souvenir Folder on Request

Let your Restricted Patients Know About

SPECIAL FOODS that SATISFY

that gnawing hunger, that craving for some forbidden delicacy, that unappeased appetite even immediately following a meal which restricted patients often suffer.

CELLU FLOUR

made of the cellulose of vegetation satisfies without nourishing. It gives bulk without food value. In filling out restricted diets this creamy, bland flour is combined with other substances which supply adhesive qualities. Because of its fine texture Cellu Flour may be found helpful where bran and other bulky substances are irritating.

Free sample of Cellu Flour sent physicians and institutions.

SPECIAL ORDERS FILLED

Special diet prescriptions for individual cases will be filled and kept on file. We are headquarters for diet materials so write us concerning restricted diet problems.

Write for our special recipes prepared by an experienced hospital dietitian. By suggesting appetizing ways for preparing permitted foods they keep chronic cases from giving up the diet struggle.

CHICAGO DIETETIC SUPPLY HOUSE, Inc.

1750-52 W. Van Buren St. - - Chicago, Illinois

Simon on Clinical Diagnosis

New (10th) Edition

By Means of Laboratory Methods

FOR A QUARTER OF A CENTURY this work has been a classic and a standard authority. The new (10th) edition further strengthens its preëminent position. *Larger by 273 pages and 21 illustrations* than the previous edition, it contains a wealth of new material and is, beyond question, the last word on *Clinical Diagnosis.*

PARASITOLOGY is today a subject of major importance and this entire section has been rewritten. It now constitutes both a useful and reliable *vade mecum* and particularly meets the wants of field workers, students and general practitioners. The section on BLOOD CHEMISTRY has been greatly enlarged and covers fully the remarkable development of those important microchemical methods introduced by Dr. Folin and his collaborators. Many changes also have been made in the section on URINE owing to the numerous and recent improvements in technic.

The section on SEROLOGY OF THE BLOOD has been entirely rewritten. The Wassermann technic, as practised and taught by Dr. Simon, as well as NOGUCHI'S two methods, have been presented in such detail that the serological beginner should find little difficulty in obtaining satisfactory results. Included also here is the latest technic suggested by SACHS-GEORGI and MEINICKE for the diagnosis of syphilis. To the description of BLOOD TYPING METHODS a special section has been devoted. The most modern and most dependable RENAL FUNCTIONAL TESTS are described and the indication for their use and their relative values discussed in detail. REHFUSS' *fractional gastric juice analysis* and LYON'S *bile studies* are fully presented.

The section on the preparation of CULTURE MEDIA—both for bacterial and protozoal work—has been much enlarged. To sum up, the book contains richly illustrated descriptions of every known morphological, physiological, chemical, pathological, parasitological, bacteriological and serological methods of the examination of the various fluids, tissues and organs of the human body, under conditions of disease. As a work of reference, it will take the place of a small library. As heretofore the first part of the book deals with technical questions, and the second with the collective presentation of the laboratory findings and their application in the various diseases under their corresponding headings.

By CHARLES E. SIMON, B.A., M.D., Professor of Clinical Pathology and Physiological Chemistry, University of Maryland Medical School and the College of Physicians and Surgeons, Baltimore, Maryland. Octavo, 1125 pages, with 233 engravings and 23 plates. Cloth, $9.00, net.

706-10 SANSOM ST. LEA & FEBIGER PHILADELPHIA

NEW (2d) EDITION

Thyroid & Thymus

By ANDRÉ CROTTI, M.D., F.A.C.S.

Formerly Professor of Clinical Surgery and Associate Professor of Anatomy, Ohio State University; Surgeon to Grant and Children's Hospital, Columbus, Ohio

Imperial De Luxe Octavo, 774 pages, with 105 illustrations and 39 colored plates. Half Morocco, $15.00, net

THE FIRST EDITION OF *"CROTTI"* was the talk of the profession and so enthusiastic its reception that it was speedily exhausted. Never had such a beautiful example of bookmaking appeared from an American press. Even more illustrations are included in this new edition, to which 204 *pages have been* added, and DR. CROTTI has subjected every page to the most searching revision and entirely rewritten many chapters. An exhaustive bibliography is included.

THE BOOK IS THE FRUIT OF OVER TWENTY YEARS' SPECIALIZATION in goiter pathology, not only in this country but also in Switzerland where the author was closely associated for years with such outstanding authorities as Professor THEODORE KOCHER, "*The Father of Goiter Surgery*," and Professor HENRY STILLING. Never have the thyroid and thymus been so exhaustively considered. All material of value in the French, Italian, German and English literature has been embodied. Thus the knowledge of the world's foremost authorities on the treatment of goiter and all diseases of the thyroid and thymus is made available. With the increasing realization of the tremendous sociological importance of hyperthyroidism, hypothyroidism and cretinism, still greater demand for the book is anticipated. The illustrations are one of the striking features, as beautiful and artistic as any that have every appeared in medical literature, they clearly visualize every operative procedure.

FULL ATTENTION HAS BEEN GIVEN to such subjects as Thyroid and Parathyroids—Postoperative Tetany—Action of Thyroid Administration and Thyroidectomy on Metabolism—Conditions Affecting the Secretions of the Thyroid Gland—How much of the Thyroid is it necessary to leave in order to prevent symptoms of thyroid insufficiency? Thyroxin—Thyroid Function and its Chemistry—Functional Interrelation of the Organs of Internal Secretion—Various Forms of Thyroiditis, including Tuberculosis, Syphilis and Woody Thyroiditis—Geographical and Racial Distribution—Economic, Social and Military Significance of Goiter and Cretinism—Theories as to Etiology—Prophylaxis—Opotherapy—Iodine—Crotti's Formula for Treatment of Non-toxic Parenchymatous Goiter—Basal Metabolism—Adrenalin Test—Iodine-Basedow—Medical Treatment of Graves's Disease, including electrotherapy, radiotherapy, serotherapy, opotherapy, etc. Under Surgical Technic the author raises and answers such questions as Excision, Resection, or Enucleation? Shall the Operation be Unilateral or Bilateral? How Much Thyroid Tissue Can Be Safely Removed? Technic of Ligation. Full technic is given for both General and Local Anesthesia. Operative Accidents and Preoperative and Postoperative treatment are thoroughly considered, as well as all the major points, as can be seen by reference to the contents on the inside pages.

706-10 Sansom St. **LEA & FEBIGER** PHILADELPHIA

Pulmonary Tuberculosis

NEW (3d) EDITION

By

MAURICE FISHBERG, M.D.

Clinical Professor of Medicine, University and Bellevue Hospital Medical College; Chief of the Tuberculosis Service, Montefiore Hospital for Chronic Diseases, and of Bedford Hill Sanatorium for Incipient Tuberculosis

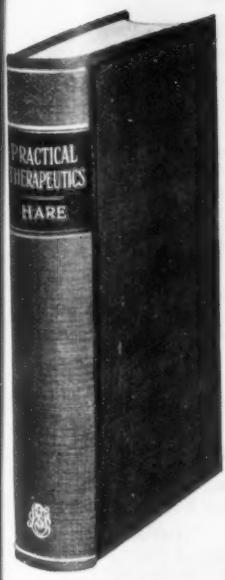
THE NEW EDITION of this standard authority is a big improvement over preceding editions. It contains 147 more pages, 32 more illustrations, and also has two new chapters of the utmost importance. That on the RECIPROCAL RELATIONS Between PULMONARY TUBERCULOSIS and CERTAIN PHYSIOLOGICAL and PATHOLOGICAL PROCESSES contains material not available in any book in any language. The other new chapter is on the MEDICO-LEGAL and INSURANCE ASPECTS of TUBERCULOSIS, and in itself is worth the price of the book to thousands of doctors engaged in insurance, indemnity, workmen's compensation and veteran rehabilitation work. Traumatic tuberculosis of late has very often been considered in the courts in claims for damages and there are many valuable passages on this point.

The former chapter discusses in full detail the reciprocal influences exercised by tuberculosis and such physiological processes as growth, puberty, sexual functions, fecundation, pregnancy, labor, the puerperium, etc. Also full consideration of the coexistence of pulmonary tuberculosis with such pathological processes as extra-thoracic tuberculous lesions, diseases of the upper respiratory tract, especially tonsillitis, coryza and the lymphatic diathesis; diseases of the bronchi and lung, notably asthma, bronchitis, bronchiectasis, emphysema, pneumonia, etc.; constitutional and metabolic diseases, such as the various forms of rheumatism, gout, diabetes, cholelithiasis, nephrolithiasis, obesity and dysfunctions of the endocrine glands, the thyroid, the adrenals and the gonads; infectious diseases, notably the exanthemata, influenza, typhoid fever, syphilis, etc.; diseases of the gastrointestinal tract, appendicitis, fistula-in-ano, cirrhosis of the liver, etc., and finally cancer and insanity. Phthisical patients often live for many years and during their period of illness are liable to suffer from various other diseases and therefore the reciprocal relations discussed in this chapter have more than theoretical bearing on the symptomatology, course and prognosis. As far as can be ascertained this is the *first attempt* to treat the subject in any book or monograph on tuberculosis.

The entire book has been reset in new type and radical changes have been made in nearly all the chapters. Those treating of Phthisiogenesis were rewritten emphasizing the problems of the constitutional *vs.* environmental factors in etiology. Also the chapter on Artificial Pneumothorax has been rewritten and amplified, limitations of this mode of treatment being pointed out. Among the many new sections that have been added the most important are on acute miliary tuberculosis, scrofula, myoidema, the autourine test, phototherapy, artificial immunization, etc.

New (3d) Edition. Octavo, 891 pages, with 129 engravings and 28 plates
Cloth, $8.50, net.

706-10 Sansom St. LEA & FEBIGER PHILADELPHIA



New (18th) Edition

A Book that has been Tested for 30 years

For 30 years this book has proved its worth in the test of daily practice. It has served over 100,000 practitioners—served them well or it wouldn't be in print. Its thirty years' usefulness has earned its reputation of being "*the dominating authority on therapeutics.*" You have in one volume your entire armamentarium and so arranged as to be instantly accessible. Every resource of medicine for the successful treatment of your patients is here. It shows *what to do and how and when to do it.*

A feature (apparently new to some works but old with Hare) is the Therapeutic Index. In one part all drugs and Remedial measures are indexed alphabetically. Then follows a list of all Diseases (also alphabetically arranged) *and under each disease* is a summary of the most approved measures for the general management of the case and then, with page references, is listed every drug or therapeutic measure of value. Thus essential information, either on a drug or disease, is secured in an instant.

Reset throughout in new type

So much of the book was rewritten that the volume has been entirely reset. There is much new material, particularly on Silver Arsphenamine, Quinidine Sulphate in Auricular Fibrillation, Thyroxin, Anterior Lobe of Pituitary, Transfusion, Intravenous Injections, Renal Disease, etc., etc.

Plan of the book

PART I, General Therapeutic Considerations, includes a number of important tables and covers Mode of Action of Drugs, Modes of Administration, Dosage, Absorption, Indications and Contraindications, Classification, Incompatibility, Prescription-writing, etc.

PART II lists all Drugs alphabetically, describing them and their physiological action, therapeutics, incompatibilities, administration, preparations, poisoning, contraindications, etc.

PART III treats of Remedial Measures other than drugs—Antiseptics, Antitoxins, Vaccines and Serums, Electro- and Hydrotherapy, Exercises, Enteroclysis, Heat and Cold, Inhalations, Intravenous Injection, Transfusion, Lavage, Lumbar Puncture, Springs and Climate, Phylacogens, Pollen Proteins, etc., always with full description of methods of procedure, indications, effects, etc.

INCLUDED in Part III is a section on Feeding the Sick and the methods of prescribing proper diet are described in more detail than in former editions, particularly in respect to children and diabetics.

IN PART IV, Treatment of Diseases, complete and definite therapeutic directions are given for all diseases. Such noted authorities as Dr. G. E. de Schweinitz, Dr. Edward Martin and Dr. Barton C. Hirst revised respectively the articles on Diseases of Eye, Venereal Diseases and Disorders of Parturition or Pregnancy.

The object of this book is to place the subject of treatment before the reader so that it may be applied at the bedside in a rational manner

By **HOBART AMORY HARE, M.D., B.Sc.,** Professor of Therapeutics, Materia Medica and Diagnosis, Jefferson Medical College; Physician to Jefferson Medical College Hospital.
Octavo, 1038 *pages, with* 144 *engravings and* 6 *plates.* *Cloth,* $6.50 *net.*

706-10 Sansom St. **LEA & FEBIGER** PHILADELPHIA

INDEX TO ADVERTISERS

TO OUR SUBSCRIBERS—only ethical products of the highest quality can be advertised in this Journal. The firms listed below merit your full confidence, all are recognized leaders in their fields. Will you kindly mention THE JOURNAL when writing them? Thank you.

Apparatus and Instruments
(Bacteriological, Diagnostic, Sterilizers, etc.)

PAGE

W. A. Baum Co. 6
Becton, Dickinson & Co.. 36
Wilmot Castle Co. 7
Eimer and Amend...2d Cover
Emil Greiner Co. 35
Charles F. Hindle & Co.. 22
Hynson, Westcott & Dunning 20
International Equip. Co.. 35
E. Leitz, Inc. 9
Precision Ther. and Instr. Co. 21
Shelton Electric Co...3d Cover
C. M. Sorensen Co. 4
Spencer Lens Co. 7
Steele Glass Co. 5
Arthur H. Thomas Co.... 3

Binders, Supporters, etc.

Katherine L. Storm, M.D. 21

Biologicals, Drugs, Pharmaceutical Supplies, etc.

Arlington Chemical Co... 15
Armour & Co. 13
E. Bilhuber, Inc. 14
G. W. Carnrick Co. 11
Ciba Co. .....4th Cover
Dermatological Research Laboratories 34
Diarsenol Co., Inc. 27
Fairchild Bros. & Foster.. 5
Hoffmann-LaRoche Chemical Works 12
Hynson, Westcott & Dunning 20
Eli Lilly & Co. 1
Loeser's Intravenous Solutions 26
Maltbie Chemical Co. ... 21
Merck & Co. 16
H. A. Metz Laboratories. 25
Parke, Davis & Co. 28
Persson Laboratories 3d Cover
Schering & Glatz, Inc.... 19
Sharp & Dohme 9
Dr. G. H. Sherman 13
Upsher Smith, Inc. 22
C. M. Sorensen Co. 4
George J. Wallau 22
Winthrop Chemical Co... 24

Foods, Beverages, etc.

Cellu Flour Mill 30
Chicago Dietetic Supply House 30
Farwell & Rhines 10
The Fleischmann Co. 2
Horlick's Malted Milk Co. 21
Joint Coffee Trade 18
Laboratory Products Co.. 8
Lister Bros., Inc. 15
Mellin's Food Co...4th Cover

Resorts and Hotels

Battle Creek Sanitarium.. 23
Chalfonte-Haddon Hall.. 29
Glen Springs 35

Sutures & Ligatures

Armour & Co. 13
Davis & Geck, Inc...2d Cover

Vibrators

Shelton Electric Co...3d Cover

X-Ray Apparatus, Tubes, etc.

Victor *X*-Ray Corp. 17

Miscellaneous

Colgate & Co. ....
Kalak Water Co. 23
Miss Harris' School 20

Publishers

Lea & Febiger 30–33
Williams & Wilkins..... 24

THE DERMATOLOGICAL RESEARCH LABORATORIES were first in the United States to produce Arsphenamine.—Due to the systematic efforts of our research staff, with laboratory facilities and personnel adapted to intensive concentration largely in this particular field, we are now producing a **NEOARSPHENAMINE** of such *low toxicity* and *high therapeutic effect* that it may be regarded as a super neoarsphenamine.

For the convenience of physicians who have not ready access to reliably distilled sterile water, we supply a bulk package (illustrated) containing 10 ampoules of any one dosage of neoarsphenamine with 10 ampoules of chemically pure sterile water, (free from organic matter). SOLUTION may be EFFECTED in the ampoule and syringe.

DERMATOLOGICAL RESEARCH INSTITUTE

(Incorporated as an Institute for Medical Research)

1720-26 LOMBARD STREET
1713-23 NAUDAIN STREET
PHILADELPHIA, PA.

Catalog
No. B202

— FINE — GLASSWARE

Apparatus for the methods of Van Slyke, Stadie, Folin, Henderson, and all bio-chemical work.

Our new Catalog "B-1" listing new apparatus in this field will be of value to every technician.

Write for your copy

THE EMIL GREINER COMPANY

MANUFACTURERS AND DEALERS
Complete Line of Laboratory Supplies
Established 1881
55 FULTON STREET NEW YORK, N. Y.

INTERNATIONAL CENTRIFUGES

ADAPTED TO
WIDE RANGE OF POWER
AND CAPACITY

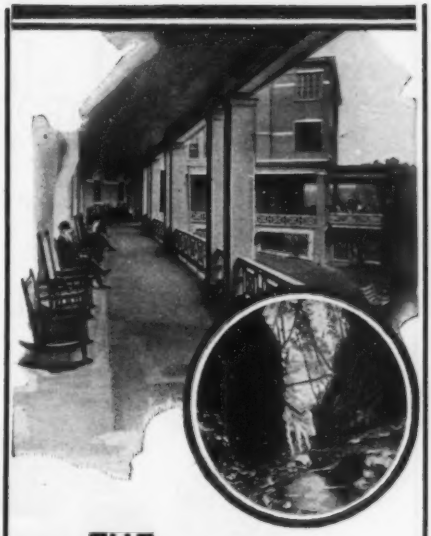
Two tubes of 15 cc. each to ten tubes of 1.3 l. each

Power 500 × gravity to 3800 × gravity

CATALOGUE C, 22 ON REQUEST

International Equipment Co.

352 Western Ave., Boston 35, Mass.



THE GLEN SPRINGS

WATKINS GLEN, N. Y., ON
SENECA LAKE

William E. Leffingwell, President

Epidemic diseases and general infection are extremely prevalent in Europe. Contact with Europeans at the various Spas abroad thus holds a particular danger for Americans.

This fact is one of many facts which serve to give such American Spas as The Glen Springs the merited attention of the profession.

The Glen Springs offers all the natural and scientific facilities of the Spas abroad, with added advantages in that the patient does not suffer the strain of an ocean trip nor lose the necessary contact with the home physician.

The closest cooperation between the professional personnel at the Glen Springs and the home physician is always maintained.

The Glen Springs is situated in the beautiful, healthful Finger Lakes region of New York State. Outdoor and indoor recreations with the charm of interesting companionship. Sporty golf course. Every luxury and comfort of a quiet delightful resort hotel.

The only place in America where the Nauheim Baths for heart and circulatory disorders are given with a natural calcium chloride brine.

OPEN THE YEAR ROUND

Illustrated and detailed booklets prepared especially for the Medical Profession on request

B-D PRODUCTS

Made for the Profession

THE FLEISCHER STETHOSCOPE

An Extremely Sensitive Stethoscope Featuring a Bracelet Attachment for Blood Pressure Determinations

***Genuine When Marked* B-D**

Supplied Only Through Dealers

BECTON, DICKINSON & CO.

RUTHERFORD, N. J.

Makers of Genuine Luer Syringes, Yale Quality Needles, **B-D** *Thermometers, Ace Bandages, Asepto Syringes, Sphygmomanometers and Spinal Manometers*

She

US

Make
quantit
milk, e
Centrif
elabora
ratus
scopic
speed c
R. P. M

SH

16 E. 42d S

THE

TH

Spe
Fron

P

Pneumo

Sepsis A
G

The follo
on reques

"Thera
"Bacte
an
"Pneu
"Specif
In

Shelton Portable Centrifuge

USED BY THE U. S. NAVY

Make your own analyses and quantitative tests of urine, milk, etc., by having a Shelton Centrifuge in your office. No elaborate installation. Apparatus held steady by gyroscopic balance wheel. Perfect speed control from 500 to 2000 R. P. M.

Write for Literature

SHELTON ELECTRIC COMPANY

16 E. 42d Street, NEW YORK CITY 30 E. Randolph Street, CHICAGO, ILL.

THE PERSSON LABORATORIES

OPERATED IN CONNECTION WITH
THE COLONIAL, MOUNT CLEMENS, MICHIGAN
(MOUNT CLEMENS SANITARIUM COMPANY)

Specific Antigens Prepared From Standardized Cultures of Known Origin

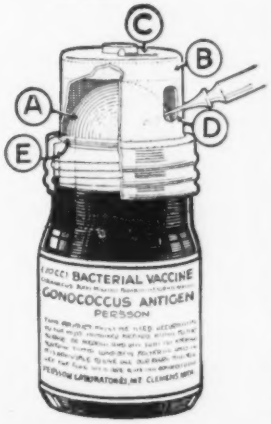
FOR THE PHYSICIAN WHO DEMANDS
ACCURATE, SCIENTIFIC THERAPY

GONOCOCCUS (Mixed) No. 35
Pneumonia Antigen No. 36
Whooping Cough Antigen No. 44
Sepsis Antigen No. 45 Rheumatic Antigen No. 38
GONOCOCCUS ANTIGEN No. 47

The following literature is available and will be mailed on request:

"Therapeutic Immunization with Bacterial Antigens"
"Bacterial Antigens in the Treatment of Gonorrheal Urethritis and its Complications"
"Pneumonia—Prophylaxis and Treatment of"
"Specific Bacterial Antigens in the Treatment of Bacterial Infections"

A-Hollow rubber stopper.
B-Aseptic pad. C-Stop for outer cap.
D-Opening for insertion of needle.
E-Flange of rubber stopper hermetically sealing bottle.



The Management of an Infant's Diet

In extreme emaciation, which is a characteristic symptom of conditions commonly known as

Malnutrition, Marasmus or Atrophy

it is difficult to give fat in sufficient amounts to satisfy the nutritive needs; therefore, it is necessary to meet this emergency by substituting some other energy-giving food element. Carbohydrates in the form of maltose and dextrins in the proportion that is found in

Mellin's Food

are especially adapted to the requirements, for such carbohydrates are readily assimilated and at once furnish heat and energy so greatly needed by these poorly nourished infants.

The method of preparing the diet and suggestions for meeting individual conditions sent to physicians upon request.

Mellin's Food Company, **Boston, Mass.**

The Premier Digitalis

Digifoline, "Ciba"

The Digitalis which gives you results when others fail

According to actual experiences of physicians DIGIFOLINE, "CIBA" *will stand this test*

Physiologically Standardized

Tablets and Liquid
For Internal Use

TRADE MARK
REGISTERED

Ampules
For Subcutaneous and Intravenous Use

Ciba Company
INCORPORATED

CEDAR AND WASHINGTON STS. NEW YORK CITY